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1. *Unstable Intermediates. Part XI.* Allylic Carbonium Ions.*

By J. Rosenbaum and M. C. R. Symons.

The ultraviolet absorption spectra of solutions thought to contain simple allylic carbonium ions, including $CH_2{:}CH{\cdot}CH_2^+$, are recorded. In most instances sulphuric acid was the solvent, and solutes included allyl alcohols and halides, diols, dienes, and epoxides. The nature of the electronic transitions is discussed and an attempt has been made to estimate pK values for allene and buta-1,3-diene.

Allylic carbonium ions are thought to be important intermediates in various acid-catalysed reactions involving allyl halides and 1,3-dienes. Whilst there is considerable kinetic evidence for their transient existence, direct methods of detection do not appear to have been used.

Since other work strongly suggests that dilute solutions of simple aliphatic carbonium ions in sulphuric acid are remarkably stable,[1,2] we have applied the same experimental techniques[3] in an attempt to prepare solutions of allylic carbonium ions in sulphuric acid.

The electronic structure of the ion $CH_2{:}CH{\cdot}CH_2^+$ has been extensively discussed since it is one of the simplest organic π-electron systems. In particular, Lefkovits, Fain, and Matsen[4] have included calculations on certain excited states for this ion, and from their results we estimate that there should be an intense band in the 250 mμ region.

Experimental and Results

Materials.—Sulphuric acid and oleums were purified as described earlier.[5] 2,4-Dimethylpenta-1,3-diene, prepared by the action of methylmagnesium iodide on mesityl oxide, had b. p. 90—93°, n^{20} 1·443. Allene, prepared by treating 2,3-dichloropropene with zinc dust and methanol, was collected in a solid carbon dioxide trap and found to be at least 90% pure by gas chromatography, the major impurity being propyne.

Other solvents and solutes were highest-grade commercial products, purified by standard methods.

The concentrations of buta-1,3-diene and allene were estimated from their ultraviolet absorption spectra in ethanol. This was accurate for butadiene, which has an intense band at 217 mμ ($\varepsilon_{max.}$ 21,000), but inaccurate for allene, for which we could detect only a rising absorption in the 220 mμ region, despite the report that there is a band of low intensity in this region for gaseous allene.[6]

Preparation of Solutions.—The reactants used, including allyl alcohol and halides, dienes,

* Part X, *Mol. Phys.*, 1960, **3**, 205.

[1] Rosenbaum and Symons, *Proc. Chem. Soc.*, 1959, 92.
[2] Rosenbaum and Symons, *Mol. Phys.*, 1960, **3**, 205.
[3] Grace and Symons, *J.*, 1959, 958.
[4] Lefkovits, Fain, and Matsen, *J. Chem. Phys.*, 1955, **23**, 1690.
[5] Symons, *J.*, 1957, 387.
[6] Lind and Livingston, *J. Amer. Chem. Soc.*, 1933, **55**, 1036.

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and the corresponding diols, are given in Table 1. The procedure for preparing stable solutions of carbonium ions was as described previously,[2,3] concentrations being generally less than 10^{-3}M.

Spectra.—Spectrophotometric measurements were made with a Unicam S.P. 500 quartz spectrophotometer and S.P. 700 recording spectrophotometer, 1 cm. stoppered cells being used whenever possible. Typical spectra are given in the Figures, and relevant details listed in Table 1. Intense bands obtained from solutions of dienes in sulphuric acid were fully developed

TABLE 1. *Details of the ultraviolet absorption spectra of compounds thought to give allylic carbonium ions in sulphuric acid* (98%).

Compound	Probable ion	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$	$\Delta\frac{1}{2}$ (cm.$^{-1}$)	Rate
$CH_2{:}CH{\cdot}CH_2{\cdot}OH$	$CH_2{:}CH{\cdot}\overset{+}{C}H_2$	273 [a]	4·7	4400	Slow
		272			
$CH_2{:}CH{\cdot}CH_2Cl$	,,	273	4·5	4900	,,
$CH_2{:}CH{\cdot}CH_2Br$	,,	275	4·2	5500	,,
$CH_2{\cdot}C_2H_3O$ *	,,	272	3·7	4400	V. slow
$CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}OH$	,,	273	3·8	4700	,,
$HO{\cdot}[CH_2]_3{\cdot}OH$	,,	271	3·7	5300	,,
$CH_2{:}\overset{+}{C}{:}CH_2$	,,	*ca.* 275	*ca.* 3·0	5600	Fast
$CH_2{:}CH{\cdot}CH{:}CH_2$	$CH_2{\cdot}\overset{+}{C}H{\cdot}CH{:}CH_2$	290	3·0	4500	Fast
$CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}CH_2{\cdot}OH$	,,	290	*ca.* 0·2	4300	V. slow
$CH_2{\cdot}CH(OH){\cdot}CH(OH){\cdot}CH_2$	,,	285	*ca.* 0·2	4700	,,
$HO{\cdot}[CH_2]_4{\cdot}OH$	,,	291	*ca.* 0·2	4500	,,
$CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}OH$	,,	290	2·5	5300	Slow
$CH_2{:}CMe{\cdot}CH_2{\cdot}OH$	$CH_2{:}CMe{\cdot}\overset{+}{C}H_2$	256	1·25	5300	Slow
$CH_2{\cdot}CH{:}CH{\cdot}CH{:}CH_2$	$CH_2{\cdot}CH{:}CH{\cdot}\overset{+}{C}H{\cdot}CH_2$	290	2·5	5000	Fast
$CH_2{\cdot}CH(OH){\cdot}CMe_2{\cdot}CHMe{\cdot}OH$	$CH_2{\cdot}CH{:}CMe{\cdot}\overset{+}{C}H{\cdot}CH_3$	305	2·5	4000	Slow
$CH_2{:}CMe{\cdot}CH{:}CH_2$	$CH_2{:}CH{\cdot}\overset{+}{C}Me_2$	300	2·3	6400	Fast
$CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}CMe_2{\cdot}OH$	$CH_2{\cdot}CH{:}CH{\cdot}\overset{+}{C}Me_2$	302	3·6	4500	Slow
$CH_2{\cdot}CH{:}CH{\cdot}CMe{:}CH_2$	,,	305	3·5	7000	Fast
$CMe_2(OH){\cdot}CMe_2{\cdot}OH$	$CMe_2{\cdot}CMe{:}\overset{+}{C}H_2$	290	1·2	5500	V. slow
$CMe_2{:}CH{\cdot}CMe{:}CH_2$	$CMe_2{:}CH{\cdot}\overset{+}{C}Me_2$	303	4·0	4600	Fast

* *I.e.*, epoxypropane.

FIG. 1. *Ultraviolet absorption spectra of* (a) *allyl alcohol and* (b) *buta-1,3-diene in sulphuric acid.*

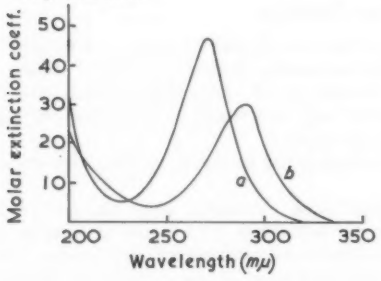
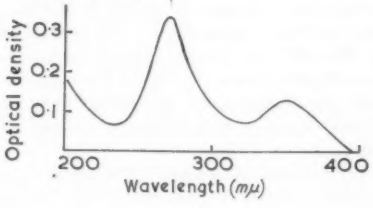


FIG. 2. *Ultraviolet absorption spectrum of a concentrated solution of allyl alcohol in sulphuric acid.*



within the time required for measurement (about 1 min.), but increased in intensity at measurable rates when solutions of hydroxy-compounds and halides were studied. However, after a period of about 3 days all spectra of dilute solutions remained constant, and data in the Table refer to such solutions.

Spectra from dilute solutions of allyl alcohol, chloride and bromide, 1,2-epoxypropane, and propane-1,2- and -1,3-diol had identical values of $\lambda_{max.}$ within experimental error, and the overall shape of the spectra were very similar to that shown in Fig. 1 for allyl alcohol. Molar extinction coefficients were all within the limits $4{\cdot}2 \pm 0{\cdot}5 \times 10^3$. The results for allene were more scattered

and it was not possible to obtain a precise value for the extinction coefficient. However, in general, the results agreed fairly closely with those for the other compounds.

Spectra of solutions more concentrated than about 10^{-3}M changed markedly with time, and a new band in the 350 mμ region generally appeared. Such a spectrum is shown in Fig. 2. No explanation for this phenomenon is offered at this stage, but whenever such a band appeared, the solutions were rejected.

Other Solvents.—Addition of dilute oleums to solutions of allyl alcohol in sulphuric acid had no effect on their spectra. The bands were also well developed when 72% perchloric acid was used as solvent, but the apparent extinction coefficients were smaller than usual.

Possibility of Oxidation.—If the carbonium ion postulate is wrong, then the spectra recorded are most probably due to oxidation products. These could have been formed by oxidation by solvent, to give sulphur dioxide, by reaction with dissolved oxygen, or by disproportionation.

Sulphur dioxide can be ruled out as a major constituent of these solutions since it has an intense band in the 200 mμ region whose long-wavelength edge should have been observed.[2] In fact, most of the spectra recorded are relatively transparent in the 200—200 mμ region and we deduce that, if sulphur dioxide is present at all, its concentration is less than 0·1 equiv.

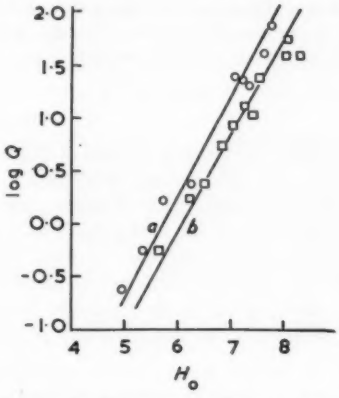


FIG. 3. *The concentration of allylic carbonium ions as a function of acidity.*

(a) *Allyl alcohol in sulphuric acid.*
(b) *Butadiene in sulphuric acid.*

Q is defined in the text. H_0 is Hammett's acidity function. The lines drawn have unit slope.

Similarly, we conclude that oxidation by dissolved oxygen is insignificant, since the bands are developed at comparable rates in the presence or absence of oxygen.

Had disproportionation occurred, the most likely reaction would have the form:

$$CH_2{:}CH{\cdot}CH_2^+ + CH_2{:}CH{\cdot}CH_2{\cdot}OH \longrightarrow CH_2{:}CHMe + CH_2{:}CH{\cdot}CH(OH)^+ \quad . \quad . \quad . \quad . \quad (1)$$

We found acraldehyde in sulphuric acid to have $\lambda_{max.}$ 238 mμ (ε 9400), and tetrahydro-2-methylfuran (which probably gives an ion $CHMe{:}CH{\cdot}CHMe^+$) in this acid to have $\lambda_{max.}$ 288 mμ (ε 380: $\Delta\frac{1}{2}$ 4500) whereas oxiran, ethane-1,2-diol, butan-2-one, dibutyl ether, methyl t-butyl ether, pivalaldehyde, and tetrahydrofuran had no strong absorption above 220 mμ. The significance of these results is outlined in the Discussion.

Acidity Functions.—A solution of allyl alcohol in sulphuric acid was stored in the dark, until there was no further change in the spectrum. Aliquot parts were withdrawn and diluted with aqueous sulphuric acids, the composition of the solutions being determined by measuring their densities and comparing them with standard tables. The spectra of these solutions were measured and the results are shown in Fig. 3, as a plot of the acidity function [7] H_0 against log Q, where Q is defined by the equation

$$Q = [\text{Carbonium}]/[\text{Olefin}] = \varepsilon_{exp.}/(\varepsilon_{max.} - \varepsilon_{exp.}) \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$\varepsilon_{exp.}$ is the apparent extinction coefficient at 272 mμ for a given H_0 value, and $\varepsilon_{max.}$ is the extinction coefficient in 98% sulphuric acid.

The results follow a line of unit slope fairly closely. Reacidification of solutions in dilute aqueous sulphuric acid with 98% sulphuric acid resulted in an immediate and quantitative reappearance of the band at 272 mμ.

[7] Deno, Jaruzelski, and Schreisheim, *J. Amer. Chem. Soc.*, 1955, **77**, 3044.

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From these results and equation (2) tentative pK values have been estimated.

$$pK_A = H_0 + \log Q \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

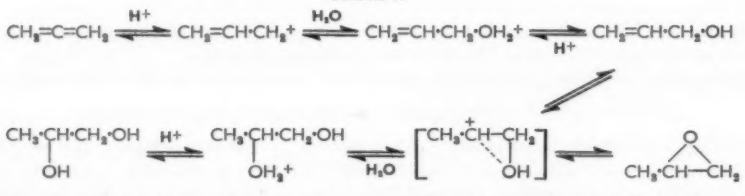
Similar results were obtained with buta-1,3-diene. The peak at 290 mμ was used to follow the spectral changes and typical results are shown in Fig. 3. Only the initial stages of deprotonation were followed since in the regions of lower acidity (<70% H_2SO_4) results were irreproducible, and a subsidiary band in the 250—260 mμ region was often found. At higher acidities, the spectral changes were reversible, and an isosbestic point appeared in the 230 mμ region. In addition a broad maximum in the 215—220 mμ region appeared, which was probably due to unprotonated butadiene. The extinction coefficient at 217 mμ, estimated on the assumption that only butadiene and its conjugate acid were present, was $1{\cdot}9 \times 10^4$: the accepted value is $2{\cdot}1 \times 10^4$. These results lend weight to the postulate that the pK values estimated from the results given in Fig. 3 are correctly assigned, namely: Me_3C^+ (ref. 2) — 3·0; $CH_2{:}CH{\cdot}CH_2^+$ — 5·5; $CH_2{:}CHMe^+$ — 5·9.

An attempt was made to measure the pK value for 2-methylpenta-1,3-diene, but in this case a band at about 260 mμ appeared as soon as the band at 305 mμ had diminished appreciably, and reacidification gave a spectrum similar to that of Fig. 2. We do not know what compound is responsible for these bands, but one can deduce from the results that the pK value must be considerably larger than that of butadiene.

Discussion

Nature of the Species with a Band at 273 mμ.—The fact that ethylene oxide and ethylene glycol do not give this species in sulphuric acid means that certain obvious explanations need not be considered. The relative rates of reaction are also significant: that olefins react very rapidly, allylic compounds at a measurable rate, and diols very slowly is in accord with the postulate that the absorbing species is, in each instance, an allylic carbonium ion (cf. Table 1), and would be difficult to explain by any other hypothesis. In this sense, these compounds resemble simple tertiary alcohols and their corresponding olefins.[1,2] Examples of the reactions postulated are summarized in Scheme 1.

Scheme 1.



Also in accord with the carbonium ion postulate are the estimated pK values, the fact that the dependence of the spectrum on acid concentration follows H_0, and the energy and intensity of the absorption band. These points are discussed in more detail below.

The most probable alternative to the carbonium-ion hypothesis, that some oxidised species is responsible for the new band, has been found (p. 3) to be unlikely.

Methyl Substitution.—Similar reasoning to that given above is applicable to the other compounds listed in Table 1, and we therefore postulate that in all cases the species responsible for the ultraviolet absorption bands are allylic carbonium ions. We conclude that methyl substitution in the β-position gives a band of slightly higher energy, whereas methyl in the α- or γ-position gives a band of lower energy, although further α- or γ-substitution has little effect.

For simplicity, the carbonium-ion postulate is accepted as correct in the following discussion.

Nature of the Electronic Transition for Allylic Carbonium Ions.—The ion, $CH_2{:}CH{\cdot}CH_2^+$, which should be planar, has C_{2v} symmetry, and the first allowed transition is expected to

be the transition, $^1A_2 \longleftarrow {}^1B_1$, which, in terms of the scheme given by Walsh for bent triatomic molecules BAB, can be written [8]

$$\ldots(b_1'')^2 \longrightarrow \ldots(b_1'')(a_2'')$$

The b_1'' level is a π molecular orbital covering all three carbon atoms: if one assumes that each carbon has sp^2-hybridization, with the directed orbitals lying in the xy plane, then the b_1'' level is built up by the in-phase overlap of the p_z-orbitals on the three carbon atoms. However, the excited a_2'' orbital is built up from out-of-phase overlap of p_z-orbitals on the two outer carbon atoms (α and γ) and is thus largely confined to these atoms. That this is the case can be seen by considering electron-spin resonance results from the allyl radical.[9] These results can be rationalised if one assumes that the unpaired electron lies almost entirely on the α- and γ-carbon atoms.[10]

We conclude that, on excitation, there will be transfer of negative charge from the β- towards the α- and γ-carbon atoms. This leads to the prediction, found to be satisfactory in another context,[3] that α- or γ-methyl substitution should lead to a strong shift of the $^1A_2 \longleftarrow {}^1B_1$ transition to shorter wavelengths, since the stabilising effect of methyl is greater, the greater the electron deficiency on the carbon to which it is attached. Similarly, we would expect β-methyl to stabilise the excited state somewhat more than the ground state, and thus shift the band slightly to longer wavelengths. These predictions are the reverse of what is observed.

If the carbonium-ion postulate is correct, then this simple viewpoint must be modified. An alternative approach would be to use data from gas-phase experiments. The ionisation potentials (in ev) for the corresponding 17-electron radicals are 8·16 for allyl,[11] 8·03 for 2-methylallyl, and 7·71 for 1-methylallyl.[12] Thus, if we correlate the energy of the $^1A_2$ excited state of the carbonium ion with the radical, we predict a steady trend (small for 2- and large for 1-methylallyl) to high energy for the $^1A_2 \longleftarrow {}^1B_1$ transition. This is now in accord with experiment for β-methyl substitution.

The result can be rationalised in terms of the correlation diagram given by Walsh.[8] We should expect that replacement of β-hydrogen by methyl would tend to decrease the apex angle. This, in turn, would lead to a *decrease* in the energy of the b_1'' level, since it is weakly bonding between the outer atoms, but an *increase* in the energy of the upper a_2''-orbital since it is antibonding between the outer atoms. If this factor is more important than the one discussed above, then a shift of the band to high energy would result.

However, all considerations show that α- or γ-substitution should give a strong shift to high energies. We therefore postulate either that the shift to low energies is a solvent effect or, more probably, that the band observed is *not* the $^1A_2 \longleftarrow {}^1B_1$ transition at all, but a transition involving the C–H bonding electrons of the substituent. The possible effect of solvent can be understood in the following way: for the allyl carbonium ion, the solvent will be organised to stabilise partial positive charges on the end carbon atoms and thus the ground state will be stabilised and the excited state destabilised relatively to the ion in the gas phase. If we consider the 1,3-dimethylallyl (1-methylbut-2-enyl) carbonium ion, the effect of solvent will be weaker, since close approach is sterically hindered, and thus, other things being equal, the band should shift to lower energies.

The alternative would be that the $^1A_2 \longleftarrow {}^1B_1$ band is, in fact, on the high-energy side of the band for the allyl ion, say in the 200 mμ region, ahd that the bands for α- or γ-methyl-substituted ions in the 300 mμ region are due to " hyperconjugation " transitions from the methyl group(s) of a type postulated already to explain the band at 293 mμ assigned to trimethyl carbonium ions, for which ordinary π–π transitions are impossible.[2]

Anomalous Extinction Coefficients.—Values of apparent extinction coefficients (ε) for

[8] Walsh, *J.*, 1953, 2266.
[9] Matheson and Smaller, *J. Chem. Phys.*, 1958, **28**, 1169.
[10] Symons, *J.*, 1959, 277.
[11] Lossing, Ingold, and Henderson, *J. Chem. Phys.*, 1954, **22**, 621.
[12] McDowell, Lossing, Henderson, and Farmer, *Canad. J. Chem.*, 1956, **34**, 345.

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bands derived from the butanediols are far smaller than those for the bands from the corresponding dienes. These bands develop very slowly, and, in general, we consider that important alternative reactions occur to give, irreversibly, compounds that have no strong bands above about 210 mμ in sulphuric acid. There are many possibilities, but the following suggestions may be relevant.

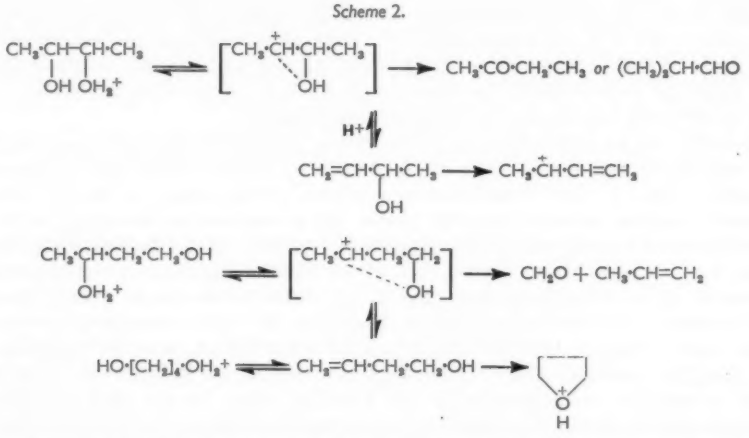
(i) Butane-1,4-diol probably gives tetrahydrofuran. Separate experiments showed that this ether does not give any band above 200 mμ even after several days in sulphuric acid. That a weak band at 291 mμ is obtained from this diol means that conversion into tetrahydrofuran is not the only reaction of significance. One reason for this could be that, in sulphuric acid, both hydroxyl groups are protonated. This would inhibit cyclisation far more than elimination. Some or all of the reactions of scheme (2) may be important.

(ii) Scheme 2 includes also the postulated reactions of butane-1,3-diol to give the carbonium ion. Again, this is a subsidiary reaction for this diol, which, in the main, reacts in other ways. We tentatively suggest that the main reaction in this instance is acid-catalysed carbon–carbon bond cleavage to give formaldehyde and propene.[13]

(iii) Similarly, butane-2,3-diol can either follow Scheme 2 to give the allylic carbonium ion or undergo rearrangement to give isobutyraldehyde or ethyl methyl ketone.

It is noteworthy that more highly substituted diols appear to give higher yields of carbonium ions. This suggests that carbonium-ion formation is facilitated by such substitution, relative to rearrangements of the type under consideration.

Scheme 2.



Significance to Reaction Mechanisms.—If our postulate is correct, then the spectral information should be of use in any studies of mechanism in which allylic carbonium ions are thought to be involved. The extinction coefficients are quite large, so that with appropriate cells it might be possible to measure the stationary concentrations of such ions during the course of reaction.

The results with epoxides are thought to be significant in connection with the question of ring opening. Ingold,[14] and Long, Pritchard, and Stafford,[15] have concluded that, at least for some epoxides in the presence of acids, carbonium ions of the type $HO{\cdot}CR_2{\cdot}CR_2^+$ are important intermediates (*A*-1 mechanism).

[13] Cf. Newman's "Steric Effects in Organic Chemistry," Wiley and Sons, New York, p. 375, for relevant references.

[14] Ingold, "Structure and Mechanism in Organic Chemistry," Bell & Sons Ltd., London, 1953, p. 344.

[15] Long, Pritchard, and Stafford, *J. Amer. Chem. Soc.*, 1957, **79**, 2362.

However, evidence from kinetic studies on solutions of epoxides under high pressure strongly suggests that even the acid-catalysed hydrolysis of isobutene oxide is a bimolecular substitution of the conjugate acid (A-2 mechanism).[16] Our results lend some support for the latter mechanism, in that there is no spectrophotometric evidence for the formation of carbonium ions of the above type which should have a spectrum rather different from those of the corresponding saturated carbonium ions.[2] Indeed, with an unprotonated hydroxyl group so close to the positive carbon atom, it is very hard to understand how cyclisation to the conjugate acid of the oxide could be avoided. Koskikallio and Whalley concluded that the Zucker–Hammett hypothesis fails in this instance.[16] Parker and Isaacs[17] have marshalled other evidence in favour of the A-2 mechanism, and suggest that most of the apparent discrepancies can be resolved if the transition state for ring opening involves a high degree of bond breaking.

Many of these arguments are relevant to the mechanism of pinacol–pinacolone rearrangements, and it seems probable that the structure of the intermediate involved will more closely resemble a protonated epoxide than a simple carbonium ion.

pK *Values.*—Since the decrease in intensity of the ultraviolet bands with decrease in acidity of the medium follows Hammett's acidity function, H_0, we conclude that the equilibrium involves gain and loss of a proton. A tentative allocation of pK values for various carbonium ions is given on p. 7. We assume that greater conjugation in the olefin accounts largely for the smaller basicity of butadiene than of isobutene and allene.

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DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHAMPTON, SOUTHAMPTON. [*Received, May 16th,* 1960.]

[16] Koskikallio and Whalley, *Trans. Faraday Soc.*, 1959, **55**, 815.
[17] Parker and Isaacs, *Chem. Rev.*, 1959, **59**, 737.

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2. *Unstable Intermediates. Part XII.* The Radical-ions* SO_2^- *and* NO_2^{2-}.

By H. C. CLARK, A. HORSFIELD, and M. C. R. SYMONS.

X-Irradiation of solid sodium or potassium dithionite results in the formation of a paramagnetic species having an ultraviolet absorption band in the 350 mμ region. This is tentatively identified as the radical-ion SO_2^-. Electron-spin resonance spectra of the irradiated solids are closely similar to that obtained from sodium dithionite moistened with water, having a g-value of 2·004 and a half-width of 11·5 gauss. A similar electron-spin resonance spectrum, obtained from the yellow solid formed by addition of excess of sodium nitrite to a solution of sodium in ammonia, is attributed to the ion NO_2^{2-}.

IN seeking to extend our studies of ions structurally similar to chlorine dioxide (19 valency electrons),[1] we have attempted to prepare the ions SO_2^- and NO_2^{2-}, and to measure their ultraviolet and electron-spin resonance spectra.

The ion SO_2^- is thought to be formed when sodium dithionite is moistened with water.[2] We have exposed crystalline sodium and potassium dithionite to X-radiation in the hope that the sulphur–sulphur bond, known to be unusually long,[3] would break homolytically, and that the resulting SO_2^- ions would remain trapped in the solid. Details of the electron

* Part XI, preceding paper.

[1] McLachlan, Symons, and Townsend, *J.*, 1959, 952.
[2] Hodgson, Neaves, and Parker, *Nature*, 1956, **178**, 489.
[3] Dunitz, *J. Amer. Chem. Soc.*, 1956, **78**, 878.

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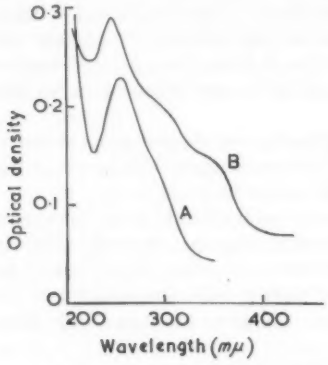
resonance spectrum of the irradiated solid, which was indistinguishable from that obtained from moist dithionite, are given in the Table. The ultraviolet spectra of powdered sodium dithionite, before and after irradiation, are given in the Figure.

The ion NO_2^{2-} is thought to be present in the yellow solid formed on addition of sodium nitrite to solutions of sodium in ammonia.[4,5] This solid is probably mainly the dimer, $Na_4N_2O_4$, but magnetic-susceptibility studies suggest that NO_2^- is a minor constituent.[5]



Spectra of solid sodium dithionite measured by diffuse reflectance methods at room temperature.
(A) *Before irradiation.* (B) *After exposure to* 50 kv X-*rays.*

Electron-spin resonance and optical spectra of various molecules and ions containing 19 *valency electrons.*

	g-Value	Δ_{MS} (gauss) *	$\lambda_{max.}$ (mμ) †	ε †
O_3^- [1]	2·012 ± 0·002	19	440	2000
NO_2^{2-}	2·003 ± 0·002	9	400	—
ClO_2 [a]	2·02,[a] 2·01 [b]	—	*ca.* 350	*ca.* 2000
SO_3^- [c]	2·005 ± 0·002	11·5	*ca.* 360	—
SO_3^- [d]	2·005 ± 0·002	11·5	—	—

* Δ_{MS} = Width between points of maximum slope taken from the first derivative of the electron-spin resonance spectra.
† For the longest-wavelength bands in the visible and ultraviolet spectra.
[a] *gx* and *gy*. [b] *gz*. [c] *X*-Irradiated $Na_2S_2O_4$. [d] Paste of $Na_2S_2O_4$ in water. [1] Bennett, Ingram, and Schonland, *Proc. Phys. Soc.*, 1956, **69**, *A*, 556.

The electron-spin resonance spectrum of this solid was similar to that for irradiated dithionite, having a *g*-value of 2·003 ± 0·001 and a width between points of maximum slope of about 9 gauss at 77° K. We were unable to measure the ultraviolet spectrum, but can infer from the colour that there is a fairly intense band with a maximum at wavelengths shorter than 400 mμ.

Experimental

Materials.—Purified anhydrous sodium dithionite was kindly supplied by Dr. C. A. Parker. Sodium nitroxylate was prepared by Zintl and Kohn's method.[4] Freshly fused and finely powdered sodium nitrite was added to a solution of purified sodium in liquid ammonia, which had been purified by distillation from metallic sodium. A bright yellow solid was formed immediately, and nitrite was added until the blue colour had been completely discharged. The solid was repeatedly washed with solvent before measurement to ensure that no metallic sodium was present. When traces of water were present during addition of nitrite, vigorous explosions occurred.

Electron-spin Resonance.—Spectra were measured at a wavelength of 3 cm., a modulation

[4] Zintl and Kohn, *Ber.*, 1928, **61**, 189.
[5] Asmussen, *Acta Chem. Scand.*, 1958, **12**, 578.

field of 10 kc./sec. and a phase-sensitive detector being used. The samples, in 5 mm. quartz tubes, were placed in an H_{102} rectangular cavity which was cooled to 77° K by immersion in liquid nitrogen. To obtain the *g*-values of the derivative spectra thus obtained, traces of diphenylpicrylhydrazyl were added. The very slight differences observed between the superimposed spectra were then estimated, and *g*-values calculated relative to $g = 2{\cdot}0032$ for diphenylpicrylhydrazyl.

Spectrophotometry.—Diffuse reflectance measurements were made directly on the powdered solids by use of a Unicam attachment fitted to an S.P. 500 spectrophotometer. To facilitate measurements in the ultraviolet region an S.Z.G. 500 photomultiplier was used as a detector, and lithium fluoride was used as a reference surface and diluent. Other precautions were used as outlined previously.[6]

X-*Irradiation.*—Polycrystalline specimens were contained in evacuated quartz tubes and irradiated for several hours with 50 kv *X*-rays at room temperature. It was established that the irradiated tubes made negligible contribution to the observed spectra.

Discussion

Identification.—That NO_2^{2-} ions are formed under the conditions described is very probable. Our results add little to the work of others, but are consistent with this postulate. Similarly, no convincing proof for the formation of SO_2^- ions has been obtained. However, the similarity between the electron-spin resonance results after *X*-irradiation and after treatment of dithionite with water, considered together with the remarkable stability of chlorine dioxide, which is isoelectronic with SO_2^-, add some weight to the postulate.

In the following, the magnetic and spectroscopic data are considered in terms of these identifications, and the effect of *X*-irradiation on dithionite is briefly discussed.

Structure.—The structure of molecules with 19 valency electrons has been discussed by Walsh,[7] and the specific case of chlorine dioxide by Bennett, Ingram, and Schonland.[8] These treatments differ in that outer *d*-orbitals on the central atom are not considered explicitly by Walsh, whereas Bennett *et al.* conclude that the b_1-orbital of chlorine dioxide, containing the unpaired electron, has about 70% 3*d*-character and 30% 3*p*-character, being almost entirely localised on chlorine.

Since the ions under consideration also have 19 electrons, they should be bent, probably with an apex angle between 110° and 120°. A simple alternative picture to that of Walsh would be that the molecule uses sp^2-hybrid orbitals on each atom to form orbitals for the σ-bonding and lone-pair electrons in the plane of the molecule. Three π-molecular orbitals can then be constructed from the remaining *p*–π orbitals on the three atoms. Of the 19 electrons, 4 would be in the σ-bonding orbitals, 10 in the σ-lone-pair orbitals, and the remaining 5 in the set of three π-orbitals. The molecule is bent because of the lone-pair of electrons on the central atom. This structure is formally similar to that of the allyl radical, which has only three π electrons. This analogy is useful because electron-spin resonance studies have shown that the outermost, unpaired electron is largely located on the end carbon atoms in the allyl radical. We can therefore say that the five π-electrons in chlorine dioxide and related ions will be distributed in such a way that the pair of lowest energy will be fairly evenly distributed on all three atoms, the next pair will be largely located on the end atoms, and the outermost unpaired electron will be located largely on the central atom. The results will be discussed in terms of these models.

Electron-spin Resonance.—The results can be compared with those obtained for NO_2,[9] O_3^-,[1] and ClO_2.[8] The hyperfine splitting from the nitrogen nucleus in NO_2 is quite large (107 gauss); and, had the splitting been at all comparable in NO_2^{2-}, a 1 : 1 : 1 triplet

[6] Griffiths, Lott, and Symons, *Analyt. Chem.*, 1959, **31**, 1338.
[7] Walsh, *J.*, 1953, 2266.
[8] Bennett, Ingram, and Schonland, *Proc. Phys. Soc.*, 1956, **69**, *A*, 556.
[9] Bird, Baird and Williams, *J. Chem. Phys.*, 1958, **28**, 738.

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should have been found rather than a single, relatively narrow line. This result is not readily understood in terms of the π-electron model given above, since the unpaired electron would be located largely on oxygen in NO_2, but largely on nitrogen in NO_2^{2-}. However, a consideration of Walsh's correlation diagram [7] suggests that, since the bond angle of NO_2 is about 140°, the a_1' level stemming from $\bar{\pi}_u$ of the linear molecular should lie above the b_2' level. This orbital tends to pure *s* on the central atom, and hence an unpaired electron in this level will have considerable *s*-character on nitrogen. This would explain the large isotropic hyperfine splitting observed. The lack of detectable splitting from NO_2^{2-} can then be understood since on either model, the orbital involved is a pure π-level, having a node at the nitrogen nucleus.

The alternative, that fine structure is lost and the line narrowed by exchange phenomena in the solid, is unlikely, since, if most of the solid is $Na_4N_2O_4$,[5] the ions NO_2^- would be suitably isolated from each other. It is nevertheless possible that the material was inhomogeneous, consisting of a mixture of Na_2NO_2 and $Na_4N_2O_4$, in which case exchange narrowing might well be important.

The *g*-values for SO_2^- and NO_2^{2-} are even closer to the free-spin value than that for O_3^- and the spectra were not very sensitive to temperature changes. We conclude that spin–orbit coupling must be very weak, despite the occurrence of a fairly intense optical absorption for each ion in the near-ultraviolet region. In this respect, these ions differ from chlorine dioxide, probably because of strong, asymmetric electric fields from the neighbouring ions in the crystals.

Optical Spectra.—Little can be said about the spectra except that the long-wavelength transitions are probably similar to the fairly intense transition of chlorine dioxide which has been described by Mulliken [10] and Walsh [7] as

$$\text{- - - - } (a_2'')(b_2')^2(a_1')^2(b_1'')^2,{}^2A_2 \longleftarrow\!\cdots\cdots (a_2'')^2(b_2')^2(a_1')^2(b_1''),{}^2B_1$$

a transition which involves movement of negative charge from oxygen towards the central atom. Experimental details are given in the Table. On the simple π-electron model, this is a π–π-transition from oxygen to the central atom.

This allocation is internally consistent except that the transition for SO_2^- would be expected to require somewhat greater energy than that for ClO_2. It is possible that the band at 300 mμ is due to the ${}^2A_2 \longleftarrow {}^2B_1$ transition of SO_2^-, superimposed upon the 300 mμ band of dithionite. In that case the shoulder at about 370 mμ remains unidentified. The other bands fit the pattern required by the postulate that there is charge transfer towards the central atom on excitation.

Dimerisation.—By measuring the electron-spin resonance spectra of solutions of chlorine dioxide at various temperatures we have found that dimerisation is unimportant even at the melting point of ethanol. In marked contrast, and despite the repulsion of like charges, SO_2^- is present almost entirely as dimer in dilute aqueous solution at room temperature. Since ClO_2 and SO_2^- are isoelectronic, this means that the major factor involved must be the decreased nuclear repulsion for $S_2O_4^{2-}$. However, although the dimer is favoured, the S–S bond is remarkably long.[3] Again, O_3^- in liquid ammonia at −80° is present entirely as monomer (no evidence for the formation of the dimer, O_6^{2-} has yet been obtained), whereas the isoelectronic ion NO_2^{2-} is thought to dimerise extensively at low temperature,[5] although our results show that this is by no means complete. Again the decreased nuclear repulsion is more important than the increased electrostatic repulsion between the ions.

X-*Irradiation of Dithionite.*—Exposure of crystals to high-energy radiation generally results in a relocation of electrons in the lattice. In alkali halide crystals the basic reaction is simply $Hal^- \longrightarrow Hal\cdot + e$, followed by the formation of Hal_2^-, Hal_2, or Hal_3^-.

The simplest fate of the electron is trapping at a halide vacancy, to give an *F*-centre.

[10] Mulliken, *Rev. Mod. Phys.*, 1942, **14**, 204.

However, when such crystals contain impurity ions, it is common to find that these ions become involved in the decomposition, and that the *final* result of irradiation is quite different, even though equation (1) may still be a good representation of the fundamental process of absorption.[11] The net result is an apparent selectivity. Similar conclusions can be drawn regarding the effect of high-energy radiation on molecular crystals and crystals containing polyatomic ions. For example, *X*-irradiation of alkali-metal nitrates gives mainly nitrites and oxygen,[12] and in a recent study of the effect of *X*-rays on potassium chlorate it is postulated that the overall process amounts to $ClO_3^- \longrightarrow ClO + O_2^-$, ClO then bonding to an adjacent chlorate ion.[13] Probably chlorite and hypochlorite ions are also formed, and identification of the paramagnetic species is not certain, but there is no evidence for the formation of *F*-centres in these studies. Since, to a good approximation, the wavelength of the *F*-band in an ionic crystal can be estimated from the lattice parameter by use of Ivey's equation,[14] $\lambda_{max.}$ (Å) $= 703a^{1.84}$, it is possible to state, on both magnetic and spectrophotometric evidence, that *F*-centres are not formed in such crystals. In general one can surmise that, for crystals containing simple cations and complex anions, after photo-ionisation has occurred, either the electron is recaptured by the electron-deficient radicals, to give " hot " ions which decompose, or that the expelled electron reacts with another anion to give break-down products.

Thus, for sodium dithionite, we can suppose that, if photo-ionisation occurs, the reaction teps may take the form

$$S_2O_4^{2-} \longrightarrow S_2O_4^- + e;\ S_2O_4^- \longrightarrow SO_2 + SO_2^-;\ S_2O_4^{2-} + e \longrightarrow SO_2^{2-} + SO_2^-,$$

rather than, or as well as, $S_2O_4^{2-} \longrightarrow 2SO_2^-$, in one step.

For ions such as nitrite, especially when in dilute " solution " in alkali halide crystals, photo-ionisation may lead to a net disproportionation:

$$2NO_2^- \longrightarrow NO_2 + NO_2^{2-}.$$

This would probably be a convenient method for preparing diluted and oriented NO_2^{2-} ions.

One of us (M. C. R. S.) thanks Professor C. A. McDowell for his kind hospitality, and the University of British Columbia for the award of a visiting Associate Professorship during the tenure of which most of this work was carried out.

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[*Received, May 16th*, 1960.]

[11] Cf. Symons and Doyle, *Quart. Rev.*, 1960, **14**, 62.
[12] Cunningham and Heal, *Trans. Faraday Soc.*, 1958, **54**, 1355.
[13] Hasty, Ard, and Moulton, *Phys. Rev.*, 1959, **116**, 1459.
[14] Ivey, *Phys. Rev.*, 1947, **72**, 341.

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3. *Unstable Intermediates. Part XIII.* Iodine Cations in Solution.*

By J. Arotsky, H. C. Mishra, and M. C. R. Symons.

Spectrophotometric, conductometric, and magnetic studies of solutions of iodine and iodine monochloride in 65% oleum show that only one iodine-containing species is formed; that the iodine is all in the +1 valency state; that the number of positive ions is equal to the number of iodine atoms; that the iodine-containing species has an intense absorption band at 640 mμ and relatively weak bands at 500 and 410 mμ; and that the effective magnetic moment is 1·5 B.M. per g.-atom of iodine.

Similar solutions have been prepared in fluorosulphonic acid and 100% sulphuric acid, but attempts to do so in sulphur trioxide, sulphuryl chloride, boron trichloride, and boron trifluoride–trifluoroacetic acid failed.

The simplest postulate is that all the iodine is converted into iodine cations having an electronic configuration $5s^25p^4$, subject to a large crystal-field stabilization and splitting of the electronic energy levels of the free cation by the surrounding solvent.

In previous papers, magnetic and spectrophotometric studies of blue solutions formed by reaction of iodine with oleum have been interpreted in terms of the formation of " free " iodine cations.[1-3] The term " free " implied that the iodine cations were not covalently bonded specifically to any nucleophile, although, in order for them to be formed at all, there must be very strong interaction with the solvent. That this must be the case can be deduced from a consideration of the changes in free energy involved.[4]

To explain the limited results then obtained, it was necessary to postulate at least two other species, namely, I_3^+, and an unidentified species containing iodine in the +1 valency state. I_3^+ was identified by comparison of the spectra of blue solutions in 65% oleum with those of brown solutions of iodine in dilute oleums.[2]

The aim of the present work was to obtain more information about these systems, particularly about the iodine cations, and to identify any other species present. Magnetic and spectrophotometric properties of solutions of iodine monochloride in various oleums and of iodine and iodine monochloride in fluorosulphonic acid and solutions of sulphur trioxide in sulphuryl chloride have been studied and conductivity in 65% oleum measured.

Experimental

Materials.—For most experiments " AnalaR " sulphuric acid was satisfactory. For spectrophotometry it was distilled, after refluxing, from potassium persulphate. This treatment decreased the optical density in the 200 mμ region to one-fifth (the O.D. at 200 mμ in a 1 cm. cell was 0·02). Oleums were prepared by addition of sulphur trioxide to purified sulphuric acid;[5] pure dry nitrogen was passed slowly through oleum previously freed from sulphur dioxide and kept at 40°, and then through sulphuric acid at 0°. Oleum concentrations were estimated by titration with water to minimum conductivity (100% H_2SO_4), a small conductivity cell fitted with short platinum wire electrodes about 4 cm. apart being used. This method was easier and more accurate than that used previously.[1]

Iodine monochloride was purified by the method of Buckles and Mills.[6]

Analyses.—The cycle from 100% sulphuric acid to concentrated oleum and back, described previously,[1] was repeated for solutions of iodine monochloride, and it was found that, in

* Part XII, preceding paper.

[1] Symons, *J.*, 1957, 387.
[2] Symons, *J.*, 1957, 2186.
[3] Connor and Symons, *J.*, 1959, 963.
[4] Bell and Gelles, *J.*, 1951, 2734.
[5] Arotsky and Symons, *Trans. Faraday Soc.*, 1960, **56**, 1426.
[6] Buckles and Mills, *J. Amer. Chem. Soc.*, 1953, **75**, 552.

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contrast to iodine, the iodine monochloride used to prepare the blue solutions was recovered quantitatively in its molecular form.

In terms of the postulate that iodine cations are formed, the reactions involved are, presumably:

$$ICl + H_2S_2O_7 + SO_3 \longrightarrow I^+ + HS_2O_7^- + H{\cdot}SO_3Cl \quad . . . . . (1)$$

$$I^+ + H{\cdot}SO_3Cl + HS_2O_7^- + 2H_2O \longrightarrow ICl + 3H_2SO_4 \quad . . . . . (2)$$

Iodine monochloride was estimated spectrophotometrically at 442 mμ, our data being very similar to those of others.[6] The cycle for iodine was repeated, and the previous results [1] were confirmed. In this instance the reaction sequence is:

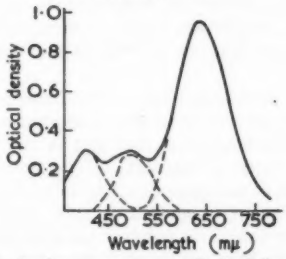
$$I_2 + H_2S_2O_7 + 3SO_3 \longrightarrow 2I^+ + SO_2 + 2HS_2O_7^- \quad . . . . . (3)$$

$$5I^+ + 8H_2O + 5HS_2O_7^- \longrightarrow 2I_2 + HIO_3 + 10H_2SO_4 \quad . . . . . (4)$$

and, provided the estimation is carried out promptly after dilution, the dissolved sulphur dioxide does not interfere.

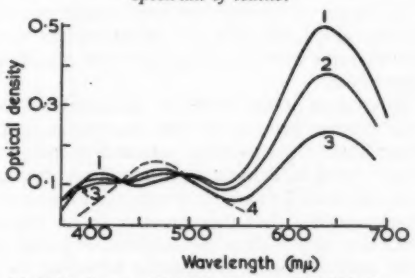
Other results which also show that all the iodine in the blue solutions is in the +1 valency state are given in the next section.

FIG. 1. *Electronic spectrum assigned to the iodine cation.*



The broken curves were derived by the method given in the Experimental section.

FIG. 2. *The effect of changing the medium on the spectrum of iodine.*



(1) 65% *oleum*; (2) 36% *oleum*; (3) 25% *oleum*; (4) *theoretical curve for* I_3^+.

Spectrophotometry.—Spectra were measured by using Unicam S.P. 500, S.P. 600, and S.P. 700 spectrophotometers. The results are summarized in Tables 1 and 2 and Figs. 1 and 2.

TABLE 1. *Spectrum assigned to the iodine cation in 65% oleum.*

10^{-3} $E_{max.}$ (cm.$^{-1}$)	1·57	2·00	2·44
10^{-2} $\varepsilon_{max.}$	18·5	4·6	4·9
10^{-4} $\Delta_{\frac{1}{2}}$ (cm.$^{-1}$)	1·23	1·50	1·70

$\Delta_{\frac{1}{2}}$ = Total width at half height.

TABLE 2. *Details of solutions of iodine and some of its compounds in various electrophilic solvents.*

Solvent	Source of iodine	Oxidant	Colour	Values for $\lambda_{max.}$ (mμ)
65% Oleum	I_2	SO_3	Blue	As Fig. 1, + band at 280 mμ (SO_2)
65% Oleum	ICl	—	Blue	As Fig. 1
H_2SO_4	I_2	HIO_3	Green	650, 460, 290
H_2SO_4	ICl	—	Brown	442, 240
$HFSO_3$	I_2	$K_2S_2O_8$	Green	642, 460
$HFSO_3$	ICl	—	Blue	—
H_2O–SO_3–SO_2Cl_2	ICl	—	Blue	645, 500, 400
HCl–BCl_3	I_2	$K_2S_2O_8$	Brown	—
BF_3–$CF_3{\cdot}CO_2H$	I_2	$K_2S_2O_8$	Brown	—
BF_3–$CF_3{\cdot}CO_2H$	ICl	—	Brown	—

Precise identification of the band maxima is rendered difficult because the bands overlap considerably. An early attempt to interpret the spectrum of iodine in 65% oleum was based

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upon the assumption that each band was symmetrical.[2] The spectra have now been analysed by assuming that each curve approximates to a Gaussian error curve with an equation:

$$\varepsilon = \varepsilon_0 \exp [-\alpha(\nu - \nu_0)^2]$$

where ε and ε_0 are the molar extinction coefficients at wave-numbers ν and ν_0 cm.$^{-1}$ respectively, ν_0 referring to the band maxima. Details are given in Table 1, and it will be seen that the bands previously thought to have maxima at 470 and 300 mμ are more accurately described by maxima at 500 and 280 mμ. Thus the original identification of this doublet as a property of I_3^+ was wrong. Absence of the 280 mμ band from solutions of iodine monochloride or iodine and iodate in oleum suggests strongly that this band is due to dissolved sulphur dioxide, which has an absorption band in this region and is extremely soluble in oleum.[7] Using 360 for the molar extinction coefficient of sulphur dioxide [7] at 280 mμ, we estimate from the spectrum of solutions of iodine in 65% oleum that the stoicheiometry is that required by equation (3) within ±10%.

A large number of spectra have been recorded over a wide range of conditions: after allowance for the presence of other bands such as those at 280 mμ for sulphur dioxide and at 290 and 460 mμ assigned to I_3^+,[2] the ratios of the optical densities for the three bands at 410, 500, and 640 mμ were constant. Thus, when the concentration of " free " sulphur trioxide was varied from 40% to 70%, when the temperature was changed from 12° to 40°, and when a large excess of various compounds such as sodium chloride, potassium pyrosulphate, or boric acid was added, the ratios of band heights were unaltered, within the limits of measurement. Other changes were observed under certain of these conditions, but we defer their discussion to a later paper.

By treating iodine with an equivalent of iodate we prepared blue solutions, characterized by the intense band in the 640 mμ region, in dilute oleums and even in 100% sulphuric acid. Similar blue solutions were obtained in anhydrous fluorosulphonic acid, but not in the other solvents listed in Table 2. Although no attempt has been made to elucidate the nature of the brown solutions formed, their appearance was similar to that of solutions of I_3^+ in sulphuric acid and we consider that this ion may be an important constituent in several of these solutions. Addition of dry sodium persulphate or iodine pentoxide to iodine in sulphur trioxide gave a yellow solid probably containing tervalent iodine; [8] but no blue colour was observed at any stage. If, however, a trace of water was also admitted into the system, a heavy, insoluble, dark blue oil separated, leaving a clear upper layer of sulphur trioxide. Similarly, the blue species was formed when water was added to solutions of iodine monochloride in sulphuryl chloride–sulphur trioxide mixtures.

Beer's law was accurately obeyed for solutions in oleum which were free from I_3^+, and the extinction coefficients given in Table 1 were calculated on the assumption that all the iodine introduced was present as monomeric, univalent iodine. That only one species is present in these solutions is also indicated by the two isosbestic points (Fig. 2) found when solutions obtained from iodine were diluted with moist sulphuric acid.

Conductance Measurements.—Conventional cells were used since the conductivity of oleum in the 65% region is about 100-fold smaller than that of 100% sulphuric acid. The cells, which have been described,[5] were fitted with a device for adding solutes and mixing solutions out of contact with the atmosphere. Cell constants were determined with aqueous potassium chloride, and the oleums were calibrated with sodium hydrogen sulphate or potassium chloride.[5] All measurements were at 25·00° ± 0·01°.

As with sulphuric acid,[5] plots of the concentration of added electrolyte against specific conductance are linear, after initial deviations. The results for a wide range of salts were independent of the nature of the added ions, and it was concluded that the observed conductivities were almost entirely due to $HS_2O_7^-$ ions, formed by reaction between solvent and solute.[5] Results obtained for iodine, iodine chloride, and potassium iodide are presented in Fig. 3. From the slopes of these plots, we deduce that for every molecule of solute, two, one, and two $HS_2O_7^-$ ions are formed, respectively, in accord with equations (1), (3), and (5).

$$I^- + 3SO_3 + H_2S_2O_7 \longrightarrow I^+ + SO_2 + 2HS_2O_7^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

[7] Gold and Tye, *J.*, 1950, 2932.

[8] Gillespie and Robinson, " Advances in Inorganic and Radiochemistry," Vol. I, p. 385, Academic Press Inc., New York, 1959.

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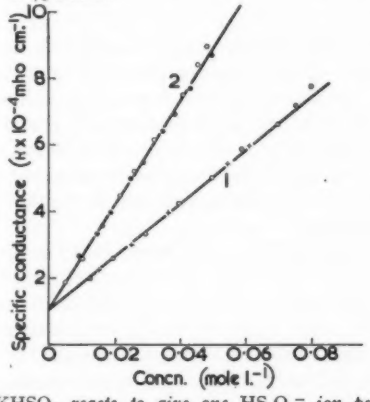
In these reactions sulphur trioxide is consumed, and a correction has been made to accommodate this, based on experiments made on a range of oleums of different strengths.[5] This correction is negligible for any but the highest concentrations reported in this work, provided the initial strength of the solvent was greater than 50%. Thus in this range of oleums, one cannot, by measurements of conductivity, detect with any accuracy a change in the composition of the medium. This is not the case for dilute oleums (<15%), and we show in a subsequent paper that use can be made of this fact to give information about solutions in dilute oleums.

In these, as in the spectrophotometric studies, it was necessary to ensure that I_3^+ was absent before concordant results were obtained. Thus, plots of the type shown in Fig. 3, constructed from data obtained from freshly prepared solutions, had slopes which were some 10—20% lower than required by theory. Spectral measurements showed that the trough between the 410 and the 500 mμ band was shallower than usual for such solutions and, with the assumption that this was due to small amounts of I_3^+ which has a band at 460 mμ, the anomalous conductivities were quantitatively accommodated.

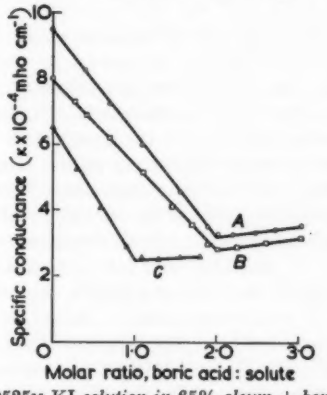
FIG. 3. *Equivalent conductance as a function of concentration of various electrolytes in 65% oleum.*



$KHSO_4$ *reacts to give one* $HS_2O_7^-$ *ion per mole;* K_2SO_4 *reacts to give two ions per mole.*

(1) { ⊙ $KHSO_4$ × ICl (2) { ○ K_2SO_4. ● KI ① I_2

FIG. 4. *Conductometric titration plots.*



(*A*) 0·0525M-KI *solution in 65% oleum + boric acid.*
(*B*) 0·043M-I_2 *solution in 65% oleum + boric acid.*
(*C*) 0·0675M-ICl *solution in 65% oleum + boric acid.*

It has been shown that boron trichloride or boric acid has a negligible effect on the conductivity of 65% oleum.[5] The resulting solutions are thought to contain $B(HS_2O_7)_3$, by analogy with reactions in sulphuric acid.[6] These solutions reacted as weak "acids" towards $HS_2O_7^-$ ions:

$$B(HS_2O_7)_3 + HS_2O_7^- \rightleftharpoons B(HS_2O_7)_4^- \quad \ldots\ldots\ldots \quad (6)$$

Thus, addition of solutions of boric acid to solutions of iodine in oleum decreased the conductivity and enabled the $HS_2O_7^-$ ions to be estimated by an independent method. Again, the results were in accord with the requirements of equations (1), (3), and (5) (cf. Fig. 4).

Magnetic Susceptibility.—A conventional Gouy susceptibility balance was used, incorporating a type A electro-magnet supplied by Newport Instruments Ltd., giving a field of 15 kgauss with a current of 10 amp. and a 2 cm. pole gap. The magnet current was stabilized to 1 part in 10^4 parts with a type B.5 power supply. A 1·0 ohm resistance was wired in series with the magnet, measurements of the potential across this resistance being used to estimate the current to 1 part in 10^4. Currents of greater than 10 amp. were used so that the magnet was saturated and small variations in current resulted in only very small fluctuations in the magnetic field. An Oertling-type 146 semimicro-balance was used to measure the force, and the sample was suspended from this with a light gold chain. The balance was calibrated with air-free water.

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The results of several measurements are given in Table 3: they are in good agreement with an estimate made from the shift in the proton resonance absorption of solutions of iodine in oleum relative to that for the pure solvent,[3] and it seems that the original estimate of 1·9 B.M. was somewhat high.[1] High precision is not possible for solutions in the concentration range

TABLE 3. *Summary of the magnetic moments assigned to the solvated iodine cation.*

Source	I_2 in 65% oleum	ICl in 65% oleum	I_2 in 65% oleum
Method	Gouy	Gouy	N.M.R.
μ (B.M.)	1·44	1·54	1·50

used previously,[1] since the estimates rest upon small differences between large weights, and diamagnetic corrections are somewhat uncertain. Therefore the data summarized in Table 3 were obtained with more concentrated solutions (0·1—1·0M).

DISCUSSION

Evidence for the Formation of the Iodine Cation.—Summarizing the results, we can assign the following properties to the blue solutions under consideration: (i) spectrophotometric results strongly suggest that there is a single constituent containing iodine, responsible for the bands at 640, 500, and 410 mμ. (ii) Analyses show conclusively that all the iodine is in the +1 valency state. (iii) Conductometric studies show that there is a single positive charge per iodine atom. (iv) Nuclear magnetic resonance studies show that this species is not protonated,[3] and also, combined with measurements of magnetic susceptibility, (v) that the species involved is paramagnetic.

These five results are all consistent with the concept that the blue species is the iodine cation, I^+, provided that interaction with solvent is such that three low-energy electronic transitions, one of considerable intensity, and an effective magnetic moment of about 1·5 B.M., can be explained. Before this is attempted, some alternatives will be discussed.

Alternative Interpretations.—Although attractive for various reasons, the species HI^+, I_2^+, I_2^{2+}, $HISO_4$, and HIS_2O_7 cannot be important constituents of the blue solutions since their properties are incompatible with one or other of results (i)—(v) above. However, the suggestion made earlier,[2] that ISO_3^+ is formed, requires detailed consideration. As will be shown below, the spectrophotometric and magnetic properties are interpretable, and each of the results (i)—(v) is accommodated, in terms of this formulation.

However, this alternative is no better than the simpler concept that solvated iodine cations are formed and the following properties of these solutions do not seem to be in accord with it. (i) Since iodine cations and sulphur trioxide are extremely powerful electrophiles, it is unlikely that they will bond strongly together, and hence (ii) it is hard to understand how ISO_3^+ can be formed in 100% sulphuric acid or fluorosulphonic acid since competing reactions between sulphur trioxide and water or hydrogen fluoride are strongly exothermic. Also, in dilute oleum, superimposed upon the normal reactions required to give iodine in the +1 valency state, reactions to give ISO_3^+ would give a readily detectable change in conductivity owing to reactions such as

$$H_2S_2O_7 + I^+ \longrightarrow H_2SO_4 + ISO_3^+ \quad . . . . . (7)$$

$$H_2S_2O_7 + H_2SO_4 \longrightarrow HS_2O_7^- + H_3SO_4^+ \quad . . . . . (8)$$

Detailed conductometric studies on solutions in dilute oleums, to be reported shortly, show that reactions (7) and (8) are insignificant. (iii) We have been unable to prepare the blue species in sulphur trioxide. This result is readily explained if this species is the iodine cation, which is unstable in the absence of a shell of polar solvent molecules, but is hard to understand if the species is ISO_3^+.

Electronic Transitions of Solvated Iodine Cations.—Since all the states of configuration

$5s^2,5p^4$ have the same parity, only quadrupole or magnetic dipole transitions are allowed. In a weak field these selection rules still hold, and the p-levels are not split by a symmetric cubic field. However, since two of the three $5p$-levels are only half filled, one would not expect to find the negative dipoles of the solvent surrounding the iodine cation exerting a symmetrical field. Rather, the filled level (p_z, say) will be avoided relative to the half-filled levels (p_x and p_y). This will tend to lower the energy of this level below that of the level in which the filled orbital is either p_x or p_y. The effect is similar to that of a linear Stark field on the $(p)^2$-configuration, and for convenience we will describe these levels as $^3\Sigma^-$ and $^3\Pi_i$ respectively.

Since the model still has inversion symmetry, $^3\Pi_i \longleftarrow {}^3\Sigma^-$ transitions are forbidden. The intensity can be greatly increased by further distortion such as to destroy the inversion symmetry, or by mixing the p-states with orbitals of opposite parity, such as the $5d$-level. Yet another way of increasing the intensity would be by charge-transfer from oriented solvent molecules.

The $^3\Pi$ level will be split into $^3\Pi_2$, $^3\Pi_1$, and $^3\Pi_0$, of which $^3\Pi_2$ should lie nearest to the ground state. According to Jevons,[9] the splitting between the $^3\Pi_2 \longrightarrow {}^3\Sigma^-$, $^3\Pi_1 \longrightarrow {}^3\Sigma^-$, and $^3\Pi_0 \longrightarrow {}^3\Sigma^-$ transitions should be equal, and approximately half the $^3P_2 - {}^3P_1$ separation for the ion in zero field.

Turning to the iodine cation, we tentatively suggest that the bands at 640, 500, and 410 mμ are in fact the three $^3\Pi_i \longrightarrow {}^3\Sigma^-$ transitions. The lowest-energy transition is far more intense than the others, as is required by theory, and the separation between the bands is 4400 cm.$^{-1}$ in each case. This is close to the value of 3600 cm.$^{-1}$ predicted from the known separation between the $^3P_2$ and $^3P_1$ levels of the free cation.[10] It therefore seems that all the spectral features assigned to the iodine cation are well accommodated by a simple model of a solvation shell in which there is close approach of, say, four molecules lying in a plane.

So far as we are aware, this is a novel application of crystal-field theory to a p-electron problem.

Magnetic Susceptibility of Iodine Cations.—The value of about 1·5 B.M. found for the iodine cation is very small for a system with two unpaired electrons. However, unexpectedly low values are also found for d-electron systems of the second- and third-row transition metals, and this has prompted us to see if the effect of a solvent field, such as that invoked to explain the spectrum of the iodine cation, might not also explain the small value found for its magnetic moment.

If we use a value of ζ, the spin-orbit coupling constant, of 3600 cm.$^{-1}$ estimated from the spectrum, then the magnetic moment μ should be, by adaptation of Kotani's theory,[11] about 1·4 B.M. at room temperature. Thus the $(p)^4$-configuration is equivalent to the $(t_{2g})^2$-configuration of transition-metal complexes. This comparison is very crude, and should be modified to accommodate the expected deviations from Russell–Saunders coupling and from cubic symmetry. However, the result strongly suggests that the low value obtained is, in fact, only to be expected for iodine cations in a strongly dipolar medium.

We conclude that all the results accumulated so far can readily be accommodated by the postulate that iodine cations are formed. However, as suggested above, the spectral results can also be explained if the ion ISO_3^+ is formed. If we neglect the possibility of π-bonding in this ion, then the effect of sulphur trioxide on the electrons of the iodine cation will be exactly the same as that outlined for the solvent field, and hence, with respect to the iodine–sulphur bond, there will be a $^3\Sigma$ and three $^3\Pi$ states as before. Thus the ion ISO_3^+ could possibly be paramagnetic and have three transitions of the type found

[9] Jevons, "Report on Band Spectra of Diatomic Molecules," Physical Society, London, 1932, p. 100.
[10] Murakawa, *Z. Physik*, 1938, **109**, 162.
[11] Kotani, *J. Phys. Soc. Japan*, 1949, **4**, 293.

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experimentally. However, in view of the chemical arguments made earlier, this postulate is not favoured.

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4. *Free-radical Substitution of Pyridine* 1-*Oxide.*

By L. K. DYALL and (the late) K. H. PAUSACKER.

Pyridine 1-oxide has been phenylated with diazoaminobenzene, and the reactivities of the nuclear positions to free-radical substitution are found to be in the order $2 > 4 > 3$. Infrared spectra of pyridine 1-oxides in the 870—710 cm.$^{-1}$ region are discussed.

THE reactivities of the three nuclear positions in pyridine 1-oxides to free-radical attack have not previously been fully determined. Colonna and Quilico [1] treated it with phenyl- and *p*-chlorophenyl-diazonium salts and isolated the 2-arylpyridine 1-oxides, but they did not mention the 3- and 4-aryl derivatives which would also be expected from a free-radical substitution.

We have treated pyridine 1-oxide with benzoyl peroxide at 100° but the yield of phenylpyridine oxides was too low to be useful: the product was largely the 2-phenyl isomer. Much better yields of phenylated product were obtained by reaction with diazoaminobenzene at 131° or 181°; the reactivities of the 2-, 4-, and 3-position being in the ratio 9·9 : 3·9 : 1. This order, $2 > 4 > 3$, follows the predictions of Barnes,[2] whose molecular-orbital calculations found the radical localisation energies, A_r, to be 2·42, 2·47, and 2·53β for the 2-, 4-, and 3-position respectively. Barnes estimated (by analogy with Brown's calculations [3] on pyridine) that a difference of 0·03β between the A_r values of two positions would correspond to a two-fold difference in rate of substitution, and the experimental values of relative reactivities agree with this estimate.

EXPERIMENTAL

M. p.s are corrected. Analyses are by the C.S.I.R.O. and University of Melbourne Microanalytical Laboratory. Light petroleum was a fraction of b. p. 55—60°.

Reagents.—Pyridine 1-oxide was prepared by oxidation of pyridine with peracetic acid.[4] The crude product was fractionated, through a 40 cm. column packed with glass helices, to remove traces of pyridine. The fraction of b. p. 110°/1 mm. was collected (Found: C, 63·5; H, 5·25; N, 15·0. Calc. for C_5H_5NO: C, 63·2; H, 5·3; N, 14·8%). Benzoyl peroxide (B.D.H.) was twice crystallised from chloroform–methanol at 0° and was dried *in vacuo* (Found: equiv., by iodometric titration, 122. Calc.: equiv., 121). Diazoaminobenzene (B.D.H.) crystallised from light petroleum (b. p. 80—100°) as golden needles, m. p. 98° (lit., 99°).

2-Phenylpyridine 1-oxide was isolated after reaction of diazoaminobenzene with pyridine 1-oxide at 181°. The crude product was isolated by chromatography in benzene on alumina. A sample was retained for infrared analysis (see run 1, Table 3); the remainder crystallised from benzene as colourless prisms, m. p. 157—158° (lit., 157°). The infrared frequencies (1600—675

[1] Colonna and Quilico, *Atti Accad. naz. Lincei, Rend. Classe. Sci. fiz. mat. nat.*, 1959, **26**, 39.
[2] Barnes, *J. Amer. Chem. Soc.*, 1959, **81**, 1935.
[3] Brown, *J.*, 1956, 272.
[4] Ochiai, *J. Org. Chem.*, 1953, **18**, 534.

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cm.$^{-1}$) and intensities in acetonitrile solution were unaltered after the sample had been further chromatographed in benzene on silica. The picrate (bright yellow needles from ethanol or toluene) had m. p. 150—151° (lit.,[5] 150—151°). 3- and 4-Phenylpyridine 1-oxide were prepared by oxidation of the appropriate phenylpyridine with peracetic acid,[6] and had m. p.s 119·5—120° (lit.,119°) and 152—153° (lit., 152·5°) respectively. The picrates had the recorded m. p.s. 4-Nitropyridine 1-oxide, m. p. 162—163° (lit., 163°), was obtained by nitration of pyridine 1-oxide,[7] and 4-ethoxypyridine 1-oxide, m. p. 32—33° (lit., 30—33°), prepared by refluxing 4-nitropyridine 1-oxide with ethanolic sodium ethoxide for 3 hr.

Infrared Spectra.—Spectra were recorded with a Perkin–Elmer Model 112 single-beam, double-pass spectrometer, with a sodium chloride prism, scanning speed 8, and 1 mm. cell thickness. Fractionated acetonitrile was used as solvent since it combines good solvent power

TABLE 1. *Infrared spectra of pyridine 1-oxides in solution.*

Subst.	—	2-Ph	3-Ph	3-Ph	4-Ph	4-NO_2	4-OEt
Solvent	MeCN	MeCN	MeCN	$CHCl_3$	MeCN	MeCN	MeCN
Concn. (mole l.$^{-1}$)	0·416	0·153	0·141	0·090	0·119	0·059	0·070
		1590 *	1608 (115)	1602 (175)	1588 * (20)	1608 (320)	1633 (100)
			1565 * (95)	1583 (55)		1591 (180)	
		1480 * (265)	1477 * (155)	1562 (100)	1478 * (445)		
		1340 (80)		1482 (150)	1312 *† (35)	1344 (520)	
				1461 † (75)			
	1327 † (10)			1422 (180)	1305 * (45)		
		1284 (30)			1290 * (50)		1289 (230)
	1256 (285)	1244 (395)	1310 (225)	1314 (235)	1254 (355)	1296 (690)	1234 (310)
	1246 † (230)		1275 * (20)		1245 †	1287 (840)	1223 (545)
			1248 *† (15)			1227 (110)	
	1195 † (40)	1185 (35)	1213 (315)	1198 * (160)	1193 † (100)	1186 † (75)	1170 (100)
			1205 †				
	1174 (145)	1158 (40)	1165 (130)	1165 (165)	1177 (295)	1171 (155)	1151 (75)
		1111 (60)	1093 *	1093 * (20)	1134 (30)	1120 (540)	1131 (120)
					1107 * (15)	1113 † (250)	
	1072 (25)	1076 * (45)	1080 *	1080 * (20)		1092 (160)	1095 (50)
			1062 * (50)				
	1020 (130)	1016 * (85)	1016 (190)	1018 (205)			
	1008 *† (20)	998 * (50)	1001 * (55)	1002 (40)	1000 * (20)		
	969 * (5)	948 * (30)	952 * (20)				
	907 * (15)		903 (220)	904 (250)			
	841 (165)	847 (200)	873 (45)	875 (75)	851 (250)	871 (310)	856 (70)
	827 † (25)		802 (83)			857 (220)	844 (140)
	774 (190)	770 ‡ (350)	766 (375)		770 (340)	753 (170)	774 (245)
		733 †	732 (125)		727 (85)		
		726 (165)			716 (82)		
		699 (220)	702 (205)		699 (150)		
	679 (145)		682 (95)			677 (100)	

* Poorly defined, being either broad and weak or obscured by solvent absorptions. † Shoulder.
‡ Asymmetry on the high-frequency side, but no shoulder.

TABLE 2. *Major peaks in the infrared spectra of pyridine 1-oxides in Nujol mulls at 880—750 cm.$^{-1}$.*

Subst.		2-Ph	3-Ph	4-Ph	4-NO_2 [15]	4-OEt
Frequencies and intensities	836s	844s	797w	855w	867s	858s
	771s	772w	759m	770m	749m	772s
		760s				

for pyridine oxides with fairly good transparency in the 1350—670 cm.$^{-1}$ region. Frequencies above 1350 cm.$^{-1}$ are only approximate. The spectrum of 3-phenylpyridine 1-oxide in chloroform solution is also reported. Apparent molar extinction coefficients, ε_A, were measured from the recorder traces, and appear accurate to $\pm 5\%$. The spectral slit widths used were 3·0 cm.$^{-1}$ at 1250 cm.$^{-1}$ and 2·5 cm.$^{-1}$ at 850 cm.$^{-1}$. The spectra are tabulated in Table 1. Table 2

[5] Edward and Gilman, *Canad. J. Chem.*, 1953, **31**, 457.
[6] Hands and Katritzky, *J.*, 1958, 1754.
[7] den Hertog and Ovenhoff, *Rec. Trav. chim.*, 1950, **69**, 468.

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reports features of the spectra of pyridine 1-oxide and some of its derivatives in Nujol mulls, recorded in the region 850—680 $cm.^{-1}$.

Phenylation with Benzoyl Peroxide.—Benzoyl peroxide (20·00 g.) was added to molten pyridine 1-oxide (149 g.) which had been saturated with carbon dioxide. The solution was heated at 100° for 3 hr., by which time evolution of carbon dioxide (0·112 mol., measured volumetrically) was complete. Crude pyridine 1-oxide (b. p. 95—105°/0·2 mm.) was recovered by distillation. This fraction was redistilled at reduced pressure from sodium carbonate, and acidification of the distillation residue yielded benzoic acid (9·45 g., 0·94 mol.), m. p. and mixed m. p. 122—123°. The first distillation residue (22·35 g.) was extracted with hot benzene. Extraction with sodium carbonate solution did not remove benzoic acid from this benzene extract. The benzene extract (16·35 g.) was refluxed for 9 hr. with potassium hydroxide (5 g.) in ethanol (150 ml.) and water (20 ml.). The solvents were distilled off, and extraction of the residue with hot benzene afforded a tar (0·73 g.). The residue was acidified, to yield benzoic acid (6·50 g., 0·64 mol.), m. p. and mixed m. p. 121—122°. The tar from the benzene extract was chromatographed in benzene on alumina, affording 63 mg. of crude material (m. p. 153—155°) whose infrared spectrum resembled that of 2-phenylpyridine 1-oxide (mixed m. p. 148—153°).

Phenylation with Diazoaminobenzene at 181°.—Diazoaminobenzene (16·50 g.) was added to molten pyridine 1-oxide (114 g.) in a vapour-jacketed vessel which was flushed out three times with dry, oxygen-free nitrogen before being heated in phenol vapour (181°). After 24 min., evolution of nitrogen started (too violently to permit collection). Gas evolution subsided after 4 min., but continued very slowly for 4 hr. Excess of pyridine 1-oxide, and aniline, were recovered from the mixture by distillation (b. p. 80—95°/0·01 mm.). The residue was further distilled, giving an orange sticky solid (6·180 g.), b. p. 131—156°/0·02 mm. The tarry residue (3·43 g.) did not distil at 240° (bath)/0·02 mm. The orange solid was chromatographed in benzene on alumina. Elution with benzene yielded a pale orange solid (4·728 g.; fraction 1), and addition of ethanol to the eluate gave a sticky yellow solid (1·277 g.; fraction 2). Crystallisation of fraction 1 from benzene–light petroleum removed highly soluble orange oils and yielded colourless needles (3·426 g.), m. p. 156—157° (Found: C, 77·5; H, 5·3. Calc. for $C_{11}H_9NO$: C, 77·3; H, 5·25%). Fraction 2 similarly crystallised to yield a colourless solid (0·548 g.) (Found: C, 77·5; H, 5·35%). The isomeric composition of each of these crystallised fractions was determined by infrared spectroscopy; the isomer ratio in the total phenylated fraction is reported in Table 3. The mother-liquors from both crystallisations were red oils from which no pure products were isolated. One or more of the strong bands in the infrared spectrum of each phenylpyridine oxide was absent from the spectra of these oils. No significant amounts of phenylpyridine oxide have therefore been lost in the crystallisations.

Phenylation with Diazoaminobenzene at 131°.—When runs were carried out as above, nitrogen evolution commenced immediately when the mixture was heated in chlorobenzene vapour (131°). The rate of nitrogen evolution was very variable. In run 2 it was steady for 3 hr. and very slow for a further 10 hr.; in run 3 it was violent for 6 min. and very slow for 5 hr.; in run 4 it was fast for 20 min. and very slow for 4 hr. The working-up procedure is described for run 4. Distillation yielded a sticky solid, b. p. 95—100°/0·2 mm., followed by orange crystals (3·229 g.), b. p. 108—148°/0·1 mm. The black amorphous residue weighed 4·56 g. The first fraction was dissolved in water (120 ml.), and extracted with benzene (3 × 120 ml.). The aqueous layer was then continuously extracted with chloroform, and the extract was distilled for recovery of pyridine 1-oxide, b. p. 102°/0·3 mm. (Found: C, 63·6; H, 5·4; N, 14·6%). The benzene extract, after drying (Na_2SO_4), yielded a pale red oil (4·19 g.), which was refluxed for 30 min. with acetic anhydride (5 ml.) and acetic acid (5 ml.). Acetanilide (2·646 g.), m. p. and mixed m. p. 114—115°, was isolated by crystallisation and sublimation. The remainder of the red oil was also examined (see next paragraph). The second distillation fraction was taken up in hot benzene (100 ml.). An insoluble red oil (0·18 g.) was separated (see next paragraph). The soluble material (3·045 g.) was chromatographed on a silica column. Benzene eluted first a red oil (1·362 g.; fraction 1), followed by a sticky solid (1·029 g.; fraction 2). Progressive addition of ethanol (up to 2% v/v) to the benzene led to elution of the remainder of the phenylated material (0·392 g.; fraction 3). Addition of 5% v/v ethanol gave pyridine 1-oxide (26 mg.) which was identified from its infrared spectrum and as picrate (m. p. and mixed m. p. 181°). From benzene–light petroleum fraction 2 gave crystals (0·850 g.) (Found: C, 77·3; H, 5·55%), whose mother-liquor was combined with fraction 1. Fraction 3 (Found:

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C, 77·7; H, 5·3%) was not crystallised. Fraction 3 and the crystalline material from fraction 2 were subjected to infrared spectroscopy; the isomer ratio in the total phenylated fraction is reported in Table 3. Fraction 1 is considered below.

TABLE 3. *Products of reactions of diazoaminobenzene with pyridine 1-oxide.*

Run no.	Temp.	Diazoaminobenzene (g.)	Reactant ratio *	Yields (mole per mole of diazoaminobenzene) N_2	Acetanilide	Phenylated	Oils †‡ (g.)	Wt. distn. residue †	2-Ph (%)	3-Ph (%)	4-Ph (%)
1	181°	16·5	14·5	—	—	0·28	0·13	0·21	79·0	7·7	13·3
2	131	16·5	18·6	0·73	0·42	0·48	0·10	0·33	76·4	8·3	15·3
3	131	11·7	18·6	—	0·32	0·07	0·24	0·41	80·9	5·6	13·5
4	131	9·1	18·5	0·78	0·43	0·16	0·20	0·50	71·3	9·6	19·2

* Moles of pyridine 1-oxide per mole of diazoaminobenzene. † G. per g. of diazoaminobenzene. ‡ These oils are those distilling in the phenylpyridine 1-oxide fraction and then isolated by chromatography.

By-products from Diazoaminobenzene Reactions.—(1) *Benzene-insoluble oils from phenylated distillation fraction.* This material was found in runs 2 (0·54 g.), 3 (0·70 g.), and 4 (0·18 g.). The oil (0·40 g.) formed a picrate (0·29 g.), m. p. 155°, from ethanol. Recrystallisation from warm ethanol yielded needles (0·19 g.), m. p. and mixed m. p. 188° with 4-phenylpyridine picrate (Found: C, 53·4; H, 3·5; N, 14·6. Calc. for $C_{17}H_{12}N_4O_7$: C, 53·2; H, 3·15; N, 14·6%).

(2) *Oils from acetylation.* Attempted sublimation at 100°/0·2 mm. of the red oil (2·38 g.) remaining after the isolation of acetanilide in run 4 resulted in distillation of an oil. This oil (0·65 g.) formed a picrate (0·63 g.), crystallising from ethanol and benzene as prisms, m. p. 164—165° (Found: C, 53·2; H, 3·2; N, 14·5%). The free base (80 mg.) was liberated from the picrate (200 mg.) by chromatography in ethanol on alumina [Found: *M* (Rast), 166. Calc. for $C_{11}H_9N$: *M*, 155]. The infrared spectrum (3500—680 cm.$^{-1}$) of a liquid film closely resembled that of 2-phenylpyridine, with a shoulder at 1540 cm.$^{-1}$ indicating the presence of a small proportion of 4-phenylpyridine.[8] The absence of a band at 810 cm.$^{-1}$ indicated that very little, if any, 3-phenylpyridine was present.[9]

(3) *Oils from chromatography.* The leading fraction from the chromatography of the phenylated fraction from each run was rechromatographed in benzene on silica. Successive elution with benzene, 1% v/v ethanol–benzene, 3% v/v ethanol–benzene, and ethanol produced four sticky orange solids in each case. The first fraction (1·10 g.) of these from run 3 yielded a crystalline picrate (0·64 g.), m. p. 162·5—164° and mixed m. p. 164° with the previous picrate of m. p. 164—165°. The infrared spectrum of a film of the oily free base confirmed the identity of this product as largely 2-phenylpyridine, with a small proportion of 4-phenylpyridine and no detectable 3-phenylpyridine. The third oily fraction (0·25 g.) afforded 4-phenylpyridine picrate (49 mg.), m. p. and mixed m. p. 188°. The second and the fourth fraction (0·08 g. and 0·10 g. respectively) could not be characterised. In all three runs at 131°, the infrared spectra of the four fractions all showed the strong 696—698 and 765—767 cm.$^{-1}$ bands of the phenyl group,[10] but important features of the spectra of all the phenylpyridine 1-oxides were absent. None of the four fractions from run 2 showed bands in the N–H stretching region (3600—3100 cm^{-1}). The oils did not contain azo-compounds since no N–H stretching bands were detected after reduction with stannous chloride in ethanolic hydrochloric acid for 5 min. at 100°.

(4) *Distillation residues.* Attempts to isolate pure products by solvent extraction, chromatography on silica and alumina, and crystallisation were unsuccessful. None of the fractions obtained formed a picrate or sublimed at 220° (bath)/0·03 mm.

Origin of Tars.—(1) *Stability of phenylpyridine 1-oxides to distillation.* A mixture of the three phenylpyridine 1-oxides (1·075 g.) was distilled (b. p. 120—140°/0·1 mm.; bath 160°), and only 28 mg. of tar remained. The isomer ratio was unchanged.

(2) *Reaction between aniline and pyridine 1-oxide.* Pyridine 1-oxide (4·32 g.) was refluxed for 6 hr. with aniline (10 ml.). Distillation afforded an oil (6·06 g.), b. p. 72—82°/2 cm. The oil was treated with acetic anhydride and acetic acid, and, after dilution with 2N-hydrochloric acid, the mixture was extracted with chloroform to remove acetanilide. The aqueous

[8] Hands and Katritzky, *J.*, 1958, 2202.
[9] Hands, Jones, and Katritzky, *J.*, 1958, 3165; Hey, Stirling, and Williams, *J.*, 1955, 3963.
[10] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 2nd edn., p. 65.

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layer was treated with excess of sodium hydrogen carbonate, and was then extracted with chloroform. Pyridine was isolated from the extract as its picrate (4 mg.). The distillation residue was shaken with benzene and water. The benzene layer yielded a black tar (0·94 g.).

A similar reaction between aniline and 2-phenylpyridine 1-oxide at 131° led neither to reduction nor to tar formation.

Infrared Determination of Isomer Ratios.—The peaks used were at 802 cm.$^{-1}$ (3-phenylpyridine 1-oxide) and 716 cm.$^{-1}$ (4-phenyl isomer); Beer's law was obeyed for each isomer. There was no suitable peak for the 2-phenyl isomer, which was determined by difference. Three synthetic isomeric mixtures, of differing compositions, were analysed. The calculated concentrations of the 3-, 4-, and 2-phenyl isomers differed from the known concentrations by averages of 4·5, 3·4, and 8·1% respectively. Corrections for overlap (which did not exceed 10% of the total absorption at either peak) were applied. Isomeric mixtures from the phenylation runs were analysed by dissolving the total sample in acetonitrile, diluting it to the required concentration, and analysing two samples. The infrared spectrum of each mixture was scanned, and the frequencies and intensities of the bands were examined to ensure that only phenylpyridine 1-oxides were present.

Complex Formation between Pyridine 1-Oxide and Diazoaminobenzene.—The infrared spectrum (calcium fluoride prism) of pyridine 1-oxide in chloroform solution (0·165M) showed the following peaks: 1606 (ε_A 95), 1487 sh (50), 1463 (840), 1410 (20), 1274 sh, and 1253 cm.$^{-1}$ (405). A 0·165M-solution of diazoaminobenzene showed peaks at 3322 (ε_A 75), 1619 (100), 1603, (585), 1516 sh (285), 1506 (400), 1481 (300), 1469 (360), 1430 (370), 1419 (145), 1310 (115), 1298 (45), 1290 (50), and 1242 cm.$^{-1}$ (555). The spectrum of a chloroform solution, 0·165M in pyridine 1-oxide and 0·164M in diazoaminobenzene, was compared with the sum of the two separate spectra: despite overlapping, the 1463 cm.$^{-1}$ peak in the pyridine 1-oxide spectrum was less intense and the 1253 cm.$^{-1}$ peak more intense. The bands at 1516, 1506, 1481, 1469, 1430, 1298, and 1290 cm.$^{-1}$ in the spectrum of diazoaminobenzene were all weaker by about 20% in the mixture. The most striking changes in the spectrum of diazoaminobenzene were at 3322 cm.$^{-1}$ (νN–H), where ε_A decreased from 75 to 45, and at 1619 cm.$^{-1}$ (δN–H), where ε_A increased from 100 to 150. The bonded N–H stretching band of diazoaminobenzene,[11] expected in the region of 3200 cm.$^{-1}$, was not sufficiently well-defined for measurement in either spectrum.

Discussion

Benzoyl Peroxide Reaction.—Extensive substitution of pyridine 1-oxide by benzoyloxy-radicals is evident from the high yield of benzoic acid (0·64 mol.) liberated on alkaline hydrolysis, and indicates[12] that pyridine 1-oxide is reactive to free-radical attack. The hydroxypyridine 1-oxides produced on hydrolysis were largely lost in aqueous extracts. Because of the unknown nature of the very extensive tar-producing side reactions, the low yield of carbon dioxide (0·11 mol.) does not necessarily support this evidence of high reactivity.

Diazoaminobenzene Reactions.—A feature of these reactions is the wide variation in yields (Table 3). The lower yields of phenylpyridine 1-oxides were accompanied by the highest yields of distillation residue and of only partly identified oils. This variability may be connected with the widely varying rates of reaction. The isomer ratio was nevertheless constant.

The yield of nitrogen (0·73—0·78 mole per mole of diazoaminobenzene) was surprisingly low, and indicates either attack by $Ph{\cdot}N_2{\cdot}$ radicals on pyridine 1-oxide or a non-homolytic side-reaction. Attempts to detect azo-compounds in the tractable products by nitrogen analysis or reduction to amines were not successful, but the tars were not examined.

Although the phenylpyridine 1-oxides were shown to resist thermal deoxygenation under the conditions used, appreciable amounts of phenylpyridines (6% from run 3) were isolated. Aniline has been stated[13] to reduce heterocyclic *N*-oxides, although it effected

[11] Dyall, *Austral. J. Chem.*, 1960, **13**, 230.
[12] Lynch and Pausacker, *Austral. J. Chem.*, 1957, **10**, 165.
[13] Katritzky, *J.*, 1956, 2404; Kloetzel and Pachter, *J. Amer. Chem. Soc.*, 1952, **74**, 971.

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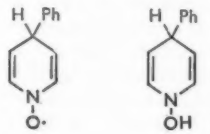
very little reduction of pyridine 1-oxide or of 2-phenylpyridine 1-oxide (the former reaction produced tars and may explain both the large production of tars and the low recovery of aniline; cf. recoveries of 0·56—0·64 mol. of aniline by Hardie and Thomson [14]). The isolation of 4-phenylpyridine picrate from a benzene-insoluble oil is particularly interesting: the solubility precludes presence of 4-phenylpyridine before treatment with picric acid. It is suggested that the radical-adduct (I) disproportionates to 4-phenylpyridine 1-oxide and the hydroxy-compound (II). The latter may be benzene-insoluble and might undergo acid-catalysed dehydration in the presence of picric acid.



(I) (II)

The relative amounts of the phenylpyridines produced were 2 > 4 > 3. Deoxygenation of some of the oxides is not likely to cause serious error in the relative reactivities calculated from the isomer composition (also 2 > 4 > 3) of the phenylpyridine 1-oxides.

The infrared spectrum of a 1 : 1 mixture of diazoaminobenzene and pyridine 1-oxide in chloroform showed fairly marked modifications in the aromatic skeletal vibrations of both components. The two compounds thus appear to form a charge-transfer complex, which is further stabilised by hydrogen bonding and, if it were stable up to the temperatures of phenylation, could lead to an isomer distribution dependent on the geometry of the complex as well as on the relative reactivities of the nuclear positions. The stability of such a complex should be temperature-dependent, and the isomer ratios at 131° and 181° would then be different if the complex survived to these temperatures. Fortunately the isomer ratio was not temperature-dependent, and it can be assumed that complex formation does not affect the reaction.

Infrared Spectra.—The position of the $^{+}N-O^{-}$ deformational band has not yet been established. Shindo [15] favours a band of strong or medium intensity at 840—870 cm.$^{-1}$ in the solid spectra of 23 of the 28 compounds he studied. Katritzky and Gardner [16] considered the 842—860 cm.$^{-1}$ band in the chloroform solution spectra of 4-substituted pyridine 1-oxides to be due to an unidentified $^{+}N-O^{-}$ vibrational mode, but Hands and Katritzky [17] assigned this band to out-of-plane C–H vibrations in the 2-substituted compounds. The 870—705 cm.$^{-1}$ region shows at least two strong bands in 27 of Shindo's compounds, and in many instances there is no reliable basis for assignment. The spectra of fifteen 4-substituted pyridine 1-oxides have been examined by Shindo [15] and the authors in the solid state, and fourteen showed strong bands at 829—705 cm.$^{-1}$ (average 770). Thirteen 3-substituted pyridine 1-oxides absorbed at 770—721 cm.$^{-1}$ (average 749), and four 2-substituted pyridine 1-oxides at 767—739 cm.$^{-1}$ (average 755). Assignment of this band to the $^{+}N-O^{-}$ deformational mode appears equally as satisfactory as the 870—840 cm.$^{-1}$ assignment. Unfortunately, bands in neither region display shifts related to the electrical effects of substituents. Both bands show a wide scatter in frequencies when the spectra of Nujol mulls are examined, and the present work (Tables 1 and 2) indicates that this scatter also occurs when the spectra are examined in solution.

The bands near 730 and 700 cm.$^{-1}$ in the spectra of the phenylpyridine 1-oxides are attributed to the phenyl group.

The surviving author is indebted to Monsanto Chemicals (Australia) for a research scholarship and thanks Professor A. N. Hambly, of Canberra University College, for his interest in the infrared spectra.

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[*Received, February 15th*, 1960.]

[14] Hardie and Thomson, *J.*, 1958, 1286.
[15] Shindo, *Chem. and Pharm. Bull.* (*Japan*), 1958, **6**, 117.
[16] Gardner and Katritzky, *J.*, 1958, 2192.
[17] Hands and Katritzky, *J.*, 1958, 2195.

XUM

5. *The Reaction of Molybdenum*(v) *Chloride with Some Aliphatic Amines.*

By D. A. Edwards and G. W. A. Fowles.

The reaction of molybdenum(v) chloride with a number of primary (NH_2R; R = Me, Et, Pr^n, and Bu^n), secondary (NHR_2; R = Me, Et, and Pr^n), and tertiary amines (NR_3; R = Me and Et) has been studied. Whereas the tertiary amines only formed simple adducts, the secondary and primary amines normally caused aminolysis of the molybdenum–chlorine bonds. In most cases the aminobasic molybdenum(v) chlorides have been isolated from the reaction products by extraction with benzene: *e.g.*, $MoCl_3(NHPr^n)_3$, $MoCl_3(NHBu^n)_2,NH_2Bu^n$, $MoCl_3(NMe_2)_2,NHMe_2$, $MoCl_3(NEt_2)_2$, and $MoCl_3(NPr^n_2)_2$.

It is known that covalent transition-metal halides are solvolysed when they react with liquid ammonia [1] or with primary or secondary amines.[2] Further, the degree of solvolysis usually decreases along the series NH_3, NH_2R, NHR_2, and the products become increasingly soluble in organic solvents; while the latter property is largely a function of the number of alkyl groups, it may also be a reflection of the formation of less polymeric products. On the other hand, simple addition compounds are usually formed between the halide and tertiary aliphatic amines,[3] although in some instances [4] the metal is reduced to a lower valency state on prolonged reaction.

Comparatively little is known of the reaction of covalent molybdenum halides with ammonia and amines. Thus cursory studies suggest that ammonolysis occurs when molybdenum(v) chloride reacts with gaseous [5] or liquid ammonia,[6] but the extent of ammonolysis is unknown. Malowan's observations [7] on the reaction of molybdenum(v) chloride with aniline and *o*-toluidine, on the other hand, are of little value because the studies were made in ethanolic solution, so that extensive solvolysis must have occurred before the amines were added. From the reaction of molybdenum(v) chloride with pyridine, Wardlaw and Webb [8] obtained several compounds of formula $MoCl_4,xPy$ (with $x = 3$, 4, and 5), in which the molybdenum atom was in a lower valency state; but the precise nature of these compounds is unknown.

In view of the sparsity of information on molybdenum–nitrogen compounds, we are making a systematic study of a number of molybdenum(v) chloride–amine systems, and in this paper we report the results of work with several primary, secondary, and tertiary aliphatic amines.

Experimental

Materials.—Molybdenum(v) chloride was prepared by the action of dry chlorine on molybdenum powder (99·9%, Messrs. Johnson, Matthey & Co. Ltd.) at 350°, and purified by sublimation (Found: Mo, 35·1; Cl, 64·6. Calc. for $MoCl_5$: Mo, 35·1, 64·9%). The amines were purified as described previously.[3] All solvents were dried over phosphoric oxide before use.

Analysis.—Analyses were carried out wherever possible; when the products were inseparable mixtures, they were usually hydrolysed *in situ* to eliminate the risk of taking a non-representative sample, so that only a Mo : Cl : N ratio is reported. Molybdenum was determined

[1] Fowles and Osborne, *J.*, 1959, 2275.
[2] Drake and Fowles, *J.*, 1960, 1498.
[3] Carnell and Fowles, *J.*, 1959, 4113.
[4] Fowles and Pleass, *J.*, 1957, 1674.
[5] Uhrlaub, *Pogg. Annalen*, 1857, **101**, 605.
[6] Bergström, *J. Amer. Chem. Soc.*, 1925, **47**, 2317.
[7] Malowan, *Arch. Pharm.*, 1930, **268**, 537.
[8] Wardlaw and Webb, *J.*, 1930, 2100.

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by oxidation to the sexivalent state, followed by reduction with mercury [9] to the quinquevalent state and final titration with cerium(IV) sulphate, ferroin being used as indicator. Chlorine was determined by potentiometric titration with silver nitrate solution, by means of a Cambridge Electro-Titration apparatus. The amine was determined by the Kjeldahl procedure.

Magnetic-susceptibility Measurements.—These were made at room temperature by Gouy's method, at a field strength of 8000 gauss. We estimate the accuracy of our measurements on solids to be of the order $\pm 0{\cdot}3$ B.M.

Molecular-weight measurements were made cryoscopically on benzene solutions, a modified form of the apparatus described previously [4] being used. Conductivity measurements were made in triply-distilled nitrobenzene that had been dried over phosphoric oxide.

Methods.—Reactions between molybdenum(v) chloride and the various amines were studied in the usual type of closed, all-glass vacuum-apparatus.[4] Initial experiments were carried out in a detachable jointed tube with stopcock. Excess of amine was condensed on to a known amount of molybdenum(v) chloride, and after about an hour at room temperature (constant shaking) the excess of amine was taken off *in vacuo* and the vessel reweighed.

Molybdenum(v) chloride was also sealed in ampoules with excess of the various amines and allowed to react for some weeks. The ampoules were then opened, the excess of amine was distilled off, and the residue analysed. Where the analysis suggested that the products might be mixtures of aminolysis products, separations were attempted by extracting the products with various organic solvents.

The reactions between molybdenum(v) chloride and mono-, di-, and tri-methylamine were also studied by passing the amine vapour (in a stream of oxygen-free nitrogen) into a solution of the chloride in carbon tetrachloride. In each case two products appeared to be formed; that which was formed initially changed colour when excess of amine was passed. The initial product was isolated by stopping the flow run at the appropriate stage.

(a) *Reaction of molybdenum*(v) *chloride with methylamine.* A greenish-brown solid and a brown solution were formed in the initial experiments, and the solid remaining after the removal of methylamine at room temperature had the overall composition $MoCl_5,5NH_2Me$ (Found: $MoCl_5 : NH_2Me = 1{\cdot}00 : 5{\cdot}02$; $1{\cdot}00 : 5{\cdot}00$). The product was heated *in vacuo* and liberated gases were trapped and identified at all temperature stages (cf. table). Above 200° hydrogen chloride was liberated and methylamine hydrochloride sublimed away.

	Temp.	25°	50°	100°	150°	200°
Amine remaining (moles/mole $MoCl_5$)	Run 1	5·02	4·96	4·65	4·10	3·91
	Run 2	5·00	4·84	4·73	4·15 *	

* Confirmed by analysis.

The paramagnetic greenish solid obtained from the ampoule reactions was $MoCl_5,7NH_2Me$ (Found: $Mo : Cl : N = 1{\cdot}00 : 5{\cdot}10 : 6{\cdot}90$; $1{\cdot}00 : 5{\cdot}00 : 7{\cdot}15$; $\mu = 2{\cdot}09$ B.M.). Although the overall analysis suggested that this product was a mixture of aminolysis products, we have been unable to find any solvent that will extract either component—benzene, 2,2,4-trimethylpentane, chlorobenzene, and methyl cyanide have been tried.

In the flow-run experiments a dark green solid was formed at first, but this became olive-green with excess of methylamine [Found (for dark green *product*): $Mo : Cl : N = 1{\cdot}00 : 4{\cdot}80 : 1{\cdot}16$; $\mu = 1{\cdot}98$ B.M. Found (for olive-green *product*): Mo, 28·4; Cl, 52·0; N, 7·96%; $\mu = 1{\cdot}74$ B.M. $MoCl_5,2NH_2Me$ requires Mo, 28·6; Cl, 52·9; N, 8·34%].

(b) *Reaction of molybdenum*(v) *chloride with other primary amines.* These were all carried out by the ampoule procedure. Molybdenum(v) chloride reacted with excess of ethylamine, n-propylamine, and n-butylamine to form brown solutions, from which a brown solid was obtained on removal of excess of amine. Analysis of the *product* of the ethylamine reaction gave: Mo, 17·3; Cl, 31·6; N, 15·5 ($MoCl_5,6NH_2Et$ requires Mo, 17·6; Cl, 32·6; N, 15·5%). Although the usual solvents were tried, no component of the mixture could be extracted.

Excess of amine was only slowly removed from the products of the n-propylamine and n-butylamine reactions, so that, although the overall composition approached $MoCl_5,6NH_2R$ in each case, this only represented the possible upper limit; thus previous work [10,11] has shown that in reactions of this kind viscous solutions are formed, and all the free amine may not be removed

[9] Furman and Murray, *J. Amer. Chem. Soc.*, 1936, **58**, 1689.
[10] Fowles and McGregor, *J.*, 1958, 136.
[11] Bannister and Fowles, *J.*, 1959, 310.

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even on prolonged pumping. The products of both reactions partly dissolved in benzene, the butylamine product being much more soluble. The aminobasic molybdenum(v) chloride $MoCl_2(NHPr^n)_3$ was first extracted from the n-propylamine *product* {Found: Mo, 27·1; Cl, 20·0; N, 12·1%; *M* (in 1·6% solution), 706. $[MoCl_2(NHPr^n)_3]_2$ requires Mo, 28·1; Cl, 20·8; N, 12·3%; *M*, 682}; it had m. p. 74° (decomp.). Even after some three washes with 50 ml. of benzene the residue was still somewhat soluble in benzene, and smaller amounts of a different compound, probably $MoCl_3(NHPr^n)_2,NH_2Pr^n$, could be extracted (Found: Mo : Cl : N = 1·00 : 3·00 : 2·68).

The molybdenum *component*, m. p. 128° (decomp.), of the n-butylamine reaction was very soluble in benzene [Found: Mo, 22·6; Cl, 24·9; N, 10·4. $MoCl_3(NHBu^n)_2,NH_2Bu^n$ requires Mo, 22·9; Cl, 25·4; N, 10·0%]. A white residue of n-butylamine hydrochloride remained (Found: N, 11·7; Cl, 32·3. Calc. for $C_4H_{12}NCl$: N, 12·7; Cl, 32·3%).

(c) *Reaction of molybdenum*(v) *chloride with dimethylamine.* The brown solid obtained from the initial reaction had an overall composition close to $MoCl_5,3NHMe_2$ (Found: $MoCl_5 : NHMe_2$ = 1·00 : 3·04). 1—2 Moles of dimethylamine hydrochloride sublimed away at 200°, leaving a brown residue of composition Mo : Cl : N = 1·00 : 3·20—3·60 : 1·30—1·60.

The product of several months' reaction in ampoules had the overall composition $MoCl_5,5NHMe_2$ (Found: Mo : Cl : N = 1·00 : 5·00 : 5·08). Part of this compound was sparingly soluble in benzene [Found: Mo : Cl : N = 1·00 : 3·10 : 3·06; *M* (in 0·11% solution), 274. $MoCl_3(NMe_2)_2,NHMe_2$ requires *M*, 336] and had m. p. 162° (decomp.).

In flow experiments, the light brown solid formed at first became very dark brown with excess of amine [Found (for the light brown *product*): Mo, 29·8; Cl, 55·0; N, 3·9. $MoCl_5,NHMe_2$ requires Mo, 30·1; Cl, 55·7; N, 4·4%. Found (for the dark brown *product*): Mo, 26·4; Cl, 49·2; N, 7·6. $MoCl_5,2NHMe_2$ requires Mo, 26·4; Cl, 48·8; N, 7·7%].

(d) *Reaction of molybdenum*(v) *chloride with other secondary amines.* Reactions with diethylamine and di-n-propylamine were carried out in ampoules, and gave products with overall compositions $MoCl_5,4NHR_2$ [Found (for the $NHEt_2$ *product*): Mo : Cl : N = 1·00 : 5·00 : 3·99. Found (for the $NHPr^n_2$ *product*): Mo, 13·6; Cl, 26·8; N, 8·3. $MoCl_5,4NHPr^n_2$ requires Mo, 14·1; Cl, 26·2; N, 8·3%]. The aminobasic molybdenum(v) chlorides $MoCl_3(NR_2)_2$ were extracted from the products with benzene {Found (for the $NHEt_2$ *product*): Mo, 26·9; Cl, 30·0; N, 8·15%; *M* (in 0·75% solution), 681. $[MoCl_3(NEt_2)_2]_2$ requires Mo, 27·7; Cl, 30·7; N, 8·1%; *M*, 693. Found (for the $NHPr^n_2$ *product*): Mo, 23·5; Cl, 26·3; N, 7·0%; *M* (in 0·87% solution), 775. $[MoCl_3(NPr^n_2)_2]_2$ requires Mo, 23·8; Cl, 26·4; N, 7·0%; *M*, 805}; m. p.s (decomp.) were 147° and 206° respectively.

(e) *Reaction of molybdenum*(v) *chloride with tertiary amines.* The slow reaction with trimethylamine (several days) gave a black solid [Found: Mo, 29·4; Cl, 54·5; N, 4·25%; *M* (in 0·13% solution), 294. $MoCl_5,NMe_3$ requires Mo, 28·9; Cl, 53·4; N, 4·2%; *M*, 332], with μ = 1·80 B.M. This *compound*, m. p. 69° (decomp.), gave a non-conducting solution in nitrobenzene. When ampoules were left for 6 months or more, a brick-red solid was formed, having μ = 1·85 B.M.; m. p. 156° (decomp.) (Found: Mo, 25·2; Cl, 45·4; N, 7·2. $MoCl_5,2NMe_3$ requires Mo, 24·5; Cl, 45·3; N, 7·2%). The *compound* is insoluble in nitrobenzene. In flow runs, a black solid (Mo : Cl : N = 1·00 : 4·75 : 0·85) was formed at first, but this became brick-red with excess of amine (Found: Mo : Cl : N = 1·00 : 4·80 : 1·80); it had μ = 1·95 B.M.

Molybdenum(v) chloride and triethylamine reacted to form a dark brown product, m. p. 178° (decomp.) [Found: Mo, 25·5; Cl, 48·0; N, 3·7%; *M* (in 0·18% solution), 407. $MoCl_5,NEt_3$ requires Mo, 25·6; Cl, 47·3; N, 3·7%; *M*, 374].

(f) The molecular weight of molybdenum(v) chloride in benzene was found to be 289 in 0·15% solution (Calc. for $MoCl_5$: *M*, 273).

Discussion

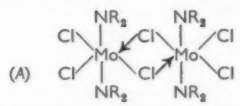
Recent *X*-ray work [12] has shown solid molybdenum(v) chloride to be dimeric with chlorine–chlorine bridges giving the molybdenum atom an octahedral configuration, but in benzene solution it is monomeric and presumably has the same trigonal–bipyramidal structure as the vapour. It is also likely to be monomeric in carbon tetrachloride, so that reactions of the chloride with amines will occur more readily in the flow runs than in the ampoule reactions where the amine has to break down the solid lattice.

[12] Zalkin and Sands, *Acta Cryst.*, 1959, **12**, 723.

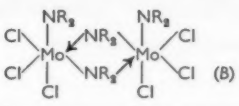
Thus trimethylamine reacts very rapidly with a solution of the chloride, giving first $MoCl_5,NMe_3$ and subsequently $MoCl_5,2NMe_3$; the same compounds are formed in the ampoule reactions, albeit more slowly: triethylamine gives only $MoCl_5,NEt_3$. In neither of the 1 : 1 compounds has molybdenum been reduced to a lower valency state, and in view of the monomeric nature of these compounds in benzene, and of the non-conducting solutions they form in nitrobenzene, it is apparent that they are simple adducts containing a co-ordinate Mo←N bond and six-covalent molybdenum. $MoCl_5,2NMe_3$, which is analogous to $MoCl_5,2OEt_2$,[8] may also be a simple adduct, and as such it would be readily formed in the flow runs; the slowness of the reaction in ampoules could be caused by the insolubility of the 1 : 1 adduct in liquid trimethylamine. The alternative formulations are less attractive. Thus ionisation, giving $[MoCl_4(NMe_3)_2]^+Cl^-$, would be unlikely to occur in the flow runs, and aminolysis is also improbable, since it requires the breaking of a strong nitrogen–carbon bond; *e.g.*, $MoCl_5,2NMe_3 = MoCl_4(NMe_2) + NMe_4Cl$. In view of the magnetic-susceptibility measurements it also seems that reduction has not occurred to any appreciable extent. It is unfortunate that the insolubility of this compound precludes further investigations.

Simple adducts again appear to be formed initially in the reactions of molybdenum(v) chloride with secondary and primary amines, since $MoCl_5,NHMe_2$ and $MoCl_5,NH_2Me$ have been isolated in flow runs. The secondary and primary amine reactions differ from the tertiary ones, however, in that solvolysis may subsequently occur very readily indeed. Because the amine concentration in the solution remains low in the flow runs, the replacement appears to stop at the first stage; the compounds ($MoCl_5$,2Amine) isolated when an excess of amine is passed in are presumably the mixtures $MoCl_4(NMe_2) + NHMe_2,HCl$ and $MoCl_4(NHMe) + NH_2Me,HCl$. With an excess of liquid amine, further replacement takes place.

The ultimate products of the prolonged reaction of molybdenum(v) chloride with dimethylamine, diethylamine, and di-n-propylamine have the overall compositions $MoCl_5,5NHMe_2$, $MoCl_5,4NHEt_2$, and $MoCl_5,4NHPr^n_2$, respectively, but these products are aminolytic mixtures from which we have been able to extract with benzene the amino-basic molybdenum(v) chlorides $MoCl_3(NMe_2)_2,NHMe_2$, $MoCl_3(NEt_2)_2$, and $MoCl_3(NPr^n_2)_2$. The dimethylamine product is monomeric, showing that the molybdenum atom achieves a co-ordination number of six through the co-ordination of a mole of dimethylamine [cf. $NbCl_3(NMe_2)_2,NHMe_2$ [13]]. However, the diethylamine and di-n-propylamine products have no co-ordinated amine, even though these higher amines are stronger bases than dimethylamine,[14] but the molybdenum atoms nevertheless attain an octahedral configuration through dimerisation. We have no direct evidence on whether the bridging is through chlorine atoms or amino-groups, and although structure (*A*) gives the more symmetrical structure, structure (*B*) is perhaps more likely since, as a Referee pointed out, the chlorine bridging in molybdenum(v) chloride breaks down in benzene solution. For the analogous alkoxy-compounds $[MoCl_3(OR)_2]_2$ Bradley *et al.*[15] favour bridging through alkoxy-groups. Larson,[16] on the other hand, who prepared analogous but polymeric compounds $[MoCl_3(O{\cdot}CO{\cdot}R)_2]_n$ by the reaction of solutions of molybdenum(v) chloride in carbon tetrachloride with several monocarboxylic acids, suggests that the chlorine–chlorine bridging of the solid chloride remains intact throughout the reaction. Since molybdenum(v) chloride is monomeric in solution, it is clear that Larson's mechanism is incorrect.



(*A*)



(*B*)

[15] Fowles and Pleass, *J.*, 1957, 2078.
[14] Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469.
[15] Bradley, Multani, and Wardlaw, *J.*, 1958, 4647.
[16] Larson, *J. Amer. Chem. Soc.*, 1960, **82**, 1223.

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When the reaction between molybdenum(v) chloride and dimethylamine is allowed to proceed for only a few hours, the product has the overall composition $MoCl_5,3NHMe_2$. This compound is probably the same as that formed in the flow runs with excess of amine, except that the molybdenum compound has taken up a mole of amine. The aminobasic molybdenum(v) chloride would be a good electron-acceptor, and the co-ordinated amine remains firmly attached on heating *in vacuo*, although decomposition sets in above 200°:

$$2MoCl_4(NMe_2),NHMe_2 \longrightarrow MoCl_4(NMe_2) + MoCl_3(NMe_2)_2 + \underbrace{NHMe_2 + HCl}_{\downarrow}$$
$$NHMe_2,HCl$$

The dimethylamine and hydrogen chloride combine on the cooler parts of the reaction vessel, making a total sublimate of 1—2 moles of dimethylamine hydrochloride, and leaving a mixture of aminobasic molybdenum(v) chlorides.

The product of the molybdenum(v) chloride–methylamine reaction, $MoCl_5,7NH_2Me$, is again undoubtedly a mixture of aminolytic products, although we have been unable to effect a separation. The magnetic-susceptibility measurements show that molybdenum is still quinquevalent, and since the degree of solvolysis must be at least as great as that with dimethylamine, the overall formula must correspond to the replacement of either two or three chlorine atoms:

(i) $MoCl_3(NHMe)_2,3NH_2Me + 2NH_2Me,HCl$
(ii) $MoCl_3(NHMe)_3,NH_2Me + 3NH_2Me,HCl$

In the initial experiments $MoCl_5,5NH_2Me$ was formed. When heated *in vacuo* to 200° this compound liberated only one mole of amine, which is in agreement with the composition $MoCl_3(NHMe)_2,NH_2Me + 2NH_2Me,HCl$, but inconsistent with any other mixture. It therefore seems likely that two chlorine atoms are replaced easily in the initial experiments, and that the third is only slowly aminolysed, giving the mixture (ii).

Ethylamine evidently reacts with molybdenum(v) chloride in the same way as methylamine, except that the aminobasic molybdenum(v) chloride no longer adds on a mole of amine:

$$i.e.,\ MoCl_5,6NH_2Et = MoCl_3(NHEt)_2 + 3NH_2Et,HCl.$$

n-Propylamine forms a mixture of molybdenum compounds, and $MoCl_2(NHPr^n)_3$ and $MoCl_3(NHPr^n)_2,NH_2Pr^n$ have been extracted from the reaction product. The first compound is dimeric in benzene solution. In the butylamine–molybdenum(v) chloride reaction the product is a simple mixture $MoCl_3(NHBu^n)_2,NH_2Bu + 2NH_2Bu^n,HCl$, from which the aminobasic molybdenum(v) chloride can be completely extracted with benzene.

The reactions of molybdenum(v) chloride with the primary amines thus show an interesting sequence in which the aminolysis decreases from methylamine to n-butylamine. Thus three molybdenum–chlorine bonds are solvolysed in methylamine and ethylamine, but the replacement of the third chlorine atom is only partly complete with n-propylamine and does not take place at all in n-butylamine. This decreasing solvolysis is a reflection of the decreasing ionising power of the amine solvents.

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6. *Polysaccharides of Baker's Yeast. Part IV.*[1] *Mannan.*

By Stanley Peat, W. J. Whelan, and T. E. Edwards.

The structure of the mannan from baker's yeast has been examined by partial acid-hydrolysis and fractionation of the products. A homologous series of oligosaccharides containing 1,6-linkages has been isolated, and the structure of the disaccharide member confirmed by chemical synthesis. The repeating linkages in these oligasaccharides are believed to have the α-configuration.

Yeast mannan is one of the three main polysaccharides of baker's yeast, the other two being glycogen [2] and the cell-wall glucan.[1,3] The mannan constitutes about 14% of the dry weight of the yeast.[4] Haworth, Hirst, and Isherwood [5] examined the structure of the mannan by methylation analysis and found the components of methylated and hydrolysed mannan to be 2,3,4,6-tetra-, 2,3,4-tri-, and 3,4-di-*O*-methylmannose in approximately equimolar ratios. Haworth, Heath, and Peat [6] later re-examined the methylated sugars and found that the tri-*O*-methyl fraction contained only 10% of the 2,3,4-isomer, the remaining 90% consisting of equimolar proportions of 2,4,6- and 3,4,6-tri-*O*-methylmannose. It was therefore concluded that the mannan contained 1,6-, 1,2- and 1,3-linkages in the proportions 2 : 3 : 1. Periodate oxidation gave results in agreement with this conclusion.[7] We have re-investigated the structure of this polysaccharide by the method we had used for the other two polysaccharide constituents, namely, partial acid-hydrolysis, fractionation, and examination of the fragments (linkage analysis).[1,3]

Previous investigators [5,6] extracted the mannan by prolonged boiling of the yeast with 6% aqueous sodium hydroxide. The mannan is, however, freely soluble in water and it seemed necessary only to disrupt the yeast cells in order to extract the polysaccharide. This was achieved by heating the yeast in an autoclave at pH 7, and the possibility of alkaline degradation was thus avoided. The extract contained glycogen and mannan, which were separated by forming the insoluble copper complex of the latter. Despite repeated purification by this method the acid-hydrolysate of the mannan always contained a trace of glucose. The polysaccharide was not stained with iodine nor did α- or β-amylase liberate maltose. The glucose did not therefore arise from glycogen and since the partial acid-hydrolysate of the mannan appeared not to contain an oligosaccharide in which glucose and mannose were combined together, it was concluded that the glucose had no structural significance in relation to the mannan but perhaps represented an impurity of cell-wall glucan.[1,3]

The mannan (33·7 g.) was hydrolysed with dilute sulphuric acid until the apparent conversion into mannose was 67%. Fractionation of the hydrolysate on charcoal–Celite yielded mannose (20·4 g.), containing a trace of glucose, and various oligosaccharides which were further fractionated where necessary in order to obtain chromatographically pure material. Also present was a non-reducing lævorotatory substance which emerged from the charcoal column just before the disaccharide fraction. In view of our finding of lævoglucosan as a product of the acid-reversion of glucose [8] it seemed likely that this material was lævomannosan. It had the same R_F value as and a similar value of $[\alpha]_D$ to authentic material. Immediately following the mannose anhydride was a reducing disaccharide (380 mg.) having a high M_G value,[9] suggestive of a 1,3- or 1,6-linkage, which

[1] Part III, *J.*, 1958, 3868.
[2] Part I, *J.*, 1955, 355.
[3] Part II, *J.*, 1958, 3862.
[4] Trevelyan and Harrison, *Biochem. J.*, 1952, **50**, 298.
[5] Haworth, Hirst, and Isherwood, *J.*, 1937, 784.
[6] Haworth, Heath, and Peat, *J.*, 1941, 833.
[7] Lindstedt, *Arkiv Kemi, Min., Geol.*, 1954, A20, No. 13.
[8] Peat, Whelan, Edwards, and Owen, *J.*, 1958, 586.
[9] Foster, *Adv. Carbohydrate Chem.*, 1957, **12**, 81.

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on periodate oxidation gave 4·8 mol. of formic acid (calc. for the 1,6-linked disaccharide, 5 mol.). The sugar had $[\alpha]_D$ +58° and formed a crystalline octa-acetate having the properties reported by Talley, Reynolds, and Evans [10] for the acetate of 6-*O*-β-D-mannopyranosyl-D-mannose, prepared by reaction between 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide and 1,2,3,4-tetra-*O*-acetyl-D-mannose. We repeated this synthesis and obtained the same product. Talley *et al.*[10] assigned the β-configuration to the linkage on the grounds that such condensation of an α-halogeno-sugar is usually accompanied by Walden inversion. However, the high $[\alpha]_D$ of the disaccharide in relation to that of mannose (+14°), and the similarly high $[\alpha]_D$ of the octa-acetate, suggested an α-linkage. The $[\alpha]_D$ of the mannan (+89°) also leads one to suspect a high content of α-linkages. Ness, Fletcher, and Hudson [11] found, moreover, that condensation of 2,3,4,6-tetra-*O*-benzoyl-α-D-mannopyranosyl bromide with methanol occurred with retention of configuration. The conclusion that the disaccharide linkage has the α-configuration has been confirmed by reports appearing since the completion of this work. Jones and Nicholson [12] obtained two 1,6-linked disaccharides as products of the acid-reversion of mannose: one of these had $[\alpha]_D$ +52°. The presence of the 1,6-link was established by methylation analysis and by periodate oxidation. This was confirmed by lead tetra-acetate oxidation,[13] and the configuration of the link established by examining the optical properties of the periodate-oxidised disaccharide.[14] The second 1,6-linked disaccharide, having $[\alpha]_D$ −12·4°, was assigned the β-configuration.[12] Gorin and Perlin [15] recently re-examined the disaccharide synthesised by the method of Talley *et al.*[10] and they too conclude that the glycosidic bond has the α-configuration.

The yeast-mannan hydrolysate contained a second disaccharide (27 mg.) which gave only glucose on hydrolysis and, on oxidation with periodate, yielded 4·75 mol. of formic acid. It had the same R_F and M_G values as gentiobiose or isomaltose. Its $[\alpha]_D$ was +22°, suggesting it was a mixture of the two glucose oligosaccharides with gentiobiose ($[\alpha]_D$ +9·6°) predominating over isomaltose ($[\alpha]_D$ +122°). It seemed that this material was to be associated with the glucan impurity and, indeed, gentiobiose is one of the products of the partial hydrolysis of yeast glucan.[3]

Only one trisaccharide (483 mg.) was isolated from the mannan hydrolysate. This formed a crystalline acetate. On the basis of the following evidence it was assigned the constitution *O*-α-D-mannopyranosyl-(1 ⟶ 6)-*O*-α-D-mannopyranosyl-(1 ⟶ 6)-D-mannose. (i) It had the same M_G value as the 1,6-linked disaccharide. (ii) Only this disaccharide and mannose were found in the products of partial acid hydrolysis of the trisaccharide. (iii) The difference in molecular rotation of the tri- and the di-saccharide acetate was the same as between the rotations of the disaccharide acetate and β-mannose penta-acetate. Finally, a tetrasaccharide (284 mg.) was obtained (from the mannan) which gave only the previously mentioned mannose tri- and di-saccharide and mannose on partial hydrolysis and seemed therefore to contain only 1,6-bonds.

The oligosaccharides larger than the tetrasaccharide (6 g.) were collected together, partly hydrolysed with acid, and refractionated. A di-, tri-, and tetra-saccharide were obtained, each having the same $[\alpha]_D$ and R_F value as the corresponding mannose oligosaccharide previously isolated. There were no glucose oligosaccharides. In addition a penta-saccharide was isolated. When partly hydrolysed with acid the tri-, tetra-, and penta-saccharide each gave mannose and one disaccharide, the latter migrating on paper chromatography with the α-1,6-linked disaccharide. That the four oligosaccharides contained the same repeating α-1,6-linkage was confirmed by the linear relations obtained

[10] Talley, Reynolds, and Evans, *J. Amer. Chem. Soc.*, 1943, **65**, 575.
[11] Ness, Fletcher, and Hudson, *J. Amer. Chem. Soc.*, 1950, **72**, 2200.
[12] Jones and Nicholson, *J.*, 1958, 27.
[13] Charlson and Perlin, *Canad. J. Chem.*, 1956, **34**, 1200.
[14] Charlson and Perlin, *Canad. J. Chem.*, 1956, **34**, 1804.
[15] Gorin and Perlin, *Canad. J. Chem.*, 1959, **37**, 1930.

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when the R_M values and the $[M]_D$ values were plotted against the degree of polymerisation.[16] The oligosaccharides larger than the pentasaccharide were collected together and examined by periodate oxidation. The limiting values for consumption of periodate and liberation of formic acid were 1·85 and 1·05 moles, respectively, per mannose unit. These values are near enough to those expected for a 1,6-linked aldohexose polymer (2 and 1 mole respectively) to suggest that the higher oligosaccharides, like the di- to penta-saccharides, contained mainly, if not entirely, 1,6-bonds.

The behaviour of the original mannan on oxidation by periodate was markedly different. In this case the limiting periodate consumption was about 1·3 moles and the acid liberated 0·35 mole per mannose unit. Clearly the polysaccharide contains a linkage or linkages other than the 1,6-bond. It seems, however, that under the conditions of hydrolysis most of these other bonds were preferentially split, giving rise, at the particular degree of hydrolysis chosen, to a series of oligosaccharides mainly containing the α-1,6-link. This is to be expected if, as in the case of glucose, the 1,6-link is the strongest of the possible glycosidic bonds. We conclude that the mannan contains sequences of α-1,6-bonds and it is possible that these form a backbone to the molecule, with side chains containing other links radiating from the main chain. The methylation analyses [5,6] agree with the presence of 1,6-links but, in addition, indicate that the molecule is highly branched.

Consideration of the products of partial acid-hydrolysis of polysaccharides must include the possibility that an oligosaccharide isolated from the hydrolysate may be the product of acid-reversion rather than a structural fragment of the polysaccharide. To determine the extent to which mannose polymerises under our conditions an approximately equivalent weight of the monosaccharide (36 g.) was treated in the same way (cf. ref. 8). Fractionation of the product on charcoal gave lævomannosan, identified as the crystalline acetate, in about two-thirds the amount obtained from the mannan. Jones and Nicholson,[12] in their studies of mannose reversion, also obtained evidence for the presence of lævomannosan. Material having the same R_F value as the α-1,6-linked disaccharide was also obtained. It is possible that this was a mixture of the α- and β-1,6-linked disaccharides, the $[\alpha]_D$ suggesting a ratio 2·7 : 1. The weight of the whole fraction was 182 mg., compared with 380 mg. of the α-1,6-linked disaccharide from the mannan, and a further 220 mg. when the mannan-derived oligosaccharides were re-hydrolysed for a short time (see Experimental section). No tri- or higher oligo-saccharide was found in the reversion products, nor did the mannan hydrolysate appear to contain any appreciable amount of the β-1,6-linked disaccharide. It seems reasonable to conclude that the di- and higher oligo-saccharides in the mannan hydrolysate came mainly from the polysaccharide and were not acid-reversion products. Jones and Nicholson [12] also obtained a 9% yield of the α-1,6-linked disaccharide from yeast mannan but did not regard the evidence as necessarily proving the presence of these bonds in the mannan.

The nature of the other linkage(s) in the mannan was not investigated in detail. A hydrolysate (mannan II; 19·6 g.; see Experimental section) in which the degree of apparent conversion into mannose was much lower (29%) was fractionated and a disaccharide (550 mg.) having R_F and M_G values different from those of the α-1,6-linked sugar was isolated. This was strongly reactive towards the benzidine–trichoroacetic acid spray for reducing sugars [17] but only weakly reactive towards alkaline silver nitrate.[18] This behaviour was later recognised to be characteristic of 1,2-linked disaccharides [18,19] and it is possible that this was 2-*O*-α-D-mannopyranosyl-D-mannose. It had $[\alpha]_D$ +48·6°, to be compared with $[\alpha]_D$ +40° for the α-1,2-disaccharide isolated by Gorin and Perlin [21] from the slime mannan produced by *Saccharomyces rouxii*.

[16] Cf. Whelan, Bailey, and Roberts, *J.*, 1953, 1293.
[17] Bacon and Edelman, *Biochem. J.*, 1951, **48**, 114.
[18] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[19] Feingold, Avigad, and Hestrin, *Biochem. J.*, 1956, **64**, 351.
[20] Haq and Whelan, *Nature*, 1956, **178**, 1222.
[21] Gorin and Perlin, *Canad. J. Chem.*, 1956, **34**, 1796.

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Experimental

General Methods.—These are described in Parts I [2] and II [3] of this series and by Peat, Whelan, and Roberts.[22] Solutions for optical rotation were in a 4 dm. tube. Whatman no. 3 MM paper was used for preparative partition chromatography. Charcoal–Celite chromatography was performed with B.D.H. "Activated charcoal for decolorizing purposes" and Celite no. 535 (Johns-Manville Co. Ltd.). All oligo- and poly-saccharide concentrations were calculated on the weight of mannose released on acid-hydrolysis in 1·5N-sulphuric acid at 100° for 3—6 hr., the Somogyi reagent [23] being used to measure the liberated mannose. A correction was made for loss of mannose owing to destruction by acid.[24] Measured with chromatographically pure mannose this was 2% after 4 hours' and 3% after 6 hours' heating. To develop full copper-reducing power mannose required 50 minutes' heating with Somogyi reagent.

Isolation of Yeast Mannan.—Baker's yeast (10 lb.; Distillers Co. Ltd.) was crumbled, stirred into 19 mM-citrate buffer (2·2 l.; pH 7·0), heated in an autoclave at 140° for 2 hr., then centrifuged and the gelatinous solid was again autoclaved with 5 l. of water. The combined extracts were concentrated under reduced pressure to 2·5 l. and made up to N in acetic acid. A brown gelatinous solid was removed on the centrifuge and washed with N-acetic acid, and the washings were added to the mannan solution which was next neutralised with 6N-sodium hydroxide and concentrated to 2 l. Ethanol (4 l.) was added and the precipitated mannan washed twice with 60% aqueous ethanol. The centrifuged solid was dissolved in water (2 l.), and a brown residue removed on the centrifuge. The cloudy supernatant solution was made alkaline with sodium hydroxide, and Fehling's solution ($CuSO_4,5H_2O$ 3·5%, Rochelle salt 1·7%, sodium hydroxide 5%) was added until the supernatant solution above the precipitated grey-blue mannan complex was deep blue and no further precipitation occurred. The complex was separated and washed several times on the centrifuge with warm water (40°). Then the complex was suspended in water (670 ml.), and concentrated hydrochloric acid was added slowly with stirring to dissolve the complex. The solution was made slightly acid and filtered through sintered-glass into ethanol (3 vol.). The white precipitate was washed with ethanol, redissolved in water (1·4 l.), and precipitated with ethanol (3 vol.). The precipitate was dissolved in water (460 ml.), and acetic acid (139 ml.) was added, followed by charcoal (5 g.). After being stirred for a few minutes the solution was centrifuged and poured into ethanol (1·85 l.). The precipitate was collected on the centrifuge and treated twice more by the same procedure. Finally the polysaccharide was dehydrated under ethanol and dried *in vacuo* over phosphoric oxide, to give 45 g. of white powder (mannan I).

In a second preparation of the mannan from 10 lb. of yeast, the copper-complex formation was repeated three times but the final precipitation from acetic acid was omitted. The yield was 24·5 g. (mannan II). Both this and the first sample gave mannose as the main component of an acid-hydrolysate, with a trace of glucose.

The first preparation was dried *in vacuo* and hydrolysed in 1·5N-sulphuric acid for 4 and for 6 hr. The reducing powers of the neutralised hydrolysates, corrected for acid-destruction of mannose (see above), corresponded to polymannose contents in the mannan of 90·0% and 89·5%, respectively. $[\alpha]_D$ of the polysaccharide, based on the carbohydrate content, was +89° (*c* 0·23).

Partial Acid-hydrolysis of Mannan I.—A small-scale hydrolysis of mannan I in 0·33N-sulphuric acid at 100° was performed to measure the rate of hydrolysis. The reducing powers at 4, 6·16, 8, and 9·5 hr. corresponded to apparent conversions into mannose of 46, 61, 68, and 74%, respectively.

Air-dried mannan I (43 g.) was heated in 0·33N-sulphuric acid (4·2 l.) in a boiling-water bath for 8 hr. After cooling, a portion (0·2 ml.) was removed for measurement of reducing power and a further portion (1 ml.) was heated in 1·5N-sulphuric acid (14·3 ml.) for 4 hr. in order to measure the total mannan content of the solution. This was 33·7 g. and the apparent conversion into mannose was 51%. The digest was again heated for 2 hr., the conversion being then 58%, and after a further 2 hr., at 67% conversion, the digest was cooled, neutralised with sodium hydroxide, and concentrated to about 500 ml.

Fractionation of Partly Hydrolysed Mannan I.—The mannan hydrolysate was adsorbed on

[22] Peat, Whelan, and Roberts, *J.*, 1957, 3916.
[23] Somogyi, *J. Biol. Chem.*, 1945, **160**, 61.
[24] Cf. Pirt and Whelan, *J. Sci. Food Agric.*, 1951, **2**, 224.

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charcoal–Celite (1 : 1 by wt.; 6 × 103 cm.) and was eluted with water. Fractions (200 ml. each) were collected and the optical rotations measured. After 36 fractions had been collected the column was eluted with 7·5% aqueous ethanol, and after fraction 76 with 15% ethanol. The fractions were combined as experience suggested and examined by paper chromatography. Fractions 52—54 (740 mg.) contained a non-reducing sugar with $R_{mannose}$ 1·50, and another sugar migrating less rapidly than mannose. By refractionation on charcoal–Celite (4 × 64 cm.) the non-reducing substance (400 mg.) was isolated. Fractions 55—60 were refractionated on charcoal–Celite (3·5 × 80 cm.). 4% Ethanol eluted more of the non-reducing substance (103 mg.), and 6% ethanol gave two separate fractions, the first *A* ($R_{mannose}$ 0·50) weighing 332 mg. and the second 280 mg. This second fraction was separated by chromatography on thick paper into three fractions *B* ($R_{mannose}$ 0·39; 27 mg.), *C* ($R_{mannose}$ 0·22; 136 mg.) and *D* ($R_{mannose}$ 0·10; 70 mg.). Further quantities of *A*, *C*, and *D* were obtained by refractionation of fractions 61—68 (990 mg.) and 69—86 (1·00 g.) on thick paper, bringing the total yields of *A*, *C*, and *D* to 380, 483, and 284 mg., respectively.

Identification of the Monosaccharides.—Fractions 21—35 (see above) contained two substances, a major component migrating with mannose and a minor component migrating with glucose. A portion (150 mg.) was fractionated on thick paper, and the major component (120 mg.) was reduced with sodium borohydride and acetylated with sodium acetate–acetic anhydride to yield mannitol hexa-acetate (229 mg., 80%), m. p. and mixed m. p. 124—125°.

Identification of 6-O-α-D-*Mannopyranosyl*-D-*mannose.*—Fraction *A* had $[\alpha]_D$ +58° in water (*c* 0·51), the concentration being determined by acid-hydrolysis to mannose, this being the only sugar detected in the hydrolysate. On oxidation in 0·185M-sodium metaperiodate at room temperature formic acid was liberated as follows: 14 hr., 4·39 mol.; 20·2 hr., 4·58; 37·7 hr., 4·65; 62·25 hr., 4·78; 72 hr., 4·78. Acetylation of the fraction (91 mg.) with anhydrous pyridine–acetic anhydride at 4° for 4 days gave an acetate (162 mg., 90%) which after three crystallisations had $[\alpha]_D$ +23·6° (*c* 0·036 in $CHCl_3$) and m. p. 151° (unchanged on admixture with synthetic disaccharide acetate, prepared as follows).

α-D-Mannopyranosyl bromide [25] (17 g.) in alcohol-free chloroform (80 ml.) was added with stirring during 1 hr. to a mixture of 1,2,3,4-tetra-*O*-acetyl-β-D-mannose [26] (16 g.), silver oxide (15 g.), calcium sulphate (50 g.; heated at 240° for 2 hr.), and iodine (2 g.) in chloroform (100 ml.).[27] After being stirred for 24 hr. the mixture was filtered through Celite and evaporated to dryness. The resulting syrup was dissolved in the minimum volume of ethanol and adsorbed on charcoal–Celite (5 × 80 cm.). An ethanol–water gradient was applied to the column, ethanol being fed into a mixing chamber containing water (15 l.) which led to the top of the column. Fractions (500 ml.) were collected, combined in pairs, evaporated to dryness, extracted with chloroform, and again recovered. Inspection of the weights of the fractions suggested that the disaccharide could be in fractions 31—38 (3 g.). These were combined and crystallised twice from ethanol. The crystals had m. p. 148—149°, $[\alpha]_D$ +22·2° (*c* 0·12 in $CHCl_3$). Talley *et al.*[10] give m. p. 152—153°, $[\alpha]_D$ +19·6°.

Examination of Fractions B, C, *and* D.—Fraction *B* gave only glucose when hydrolysed with acid (evidence of paper chromatography). It had $[\alpha]_D$ +22° (*c* 0·032 in H_2O). On oxidation with periodate as for fraction *A*, the yields of formic acid after 62·5 and 87 hr. were 4·50 and 4·75 mol., respectively. The sugar had the same R_F and M_G values as gentiobiose and isomaltose.

Fraction *C* was partly hydrolysed with acid and examined by paper chromatography. Apart from unchanged material the hydrolysate contained substances with the R_F values of mannose and fraction *A*. The sugar had $[\alpha]_D$ +68° (*c* 0·42 in H_2O). On acetylation with pyridine–acetic anhydride at 4° an acetate was obtained which after three crystallisations from ethanol had m. p. 162—163° and $[\alpha]_D$ +43·7° (*c* 0·09 in $CHCl_3$).

Fraction *D* ($[\alpha]$ +70°) was partly hydrolysed with acid, and substances migrating with fractions *C*, *A*, and mannose were then seen on a paper chromatogram.

Partial Hydrolysis and Fractionation of Mannose Oligosaccharides.—Fractions 87—108 obtained in the separation of the partly hydrolysed mannan (see above) were found by paper chromatography to consist of sugars with $R_{mannose}$ <0·1. Partial acid-hydrolysis of a small portion gave substances migrating with mannose and fractions *A*, *C*, and *D*. Fraction *B* and

[25] Brauns, *J. Res. Nat. Bur. Stand.*, 1931, **7**, 573.
[26] Reynolds and Evans, *J. Amer. Chem. Soc.*, 1940, **62**, 66.
[27] Evans, Reynolds, and Talley, *Adv. Carbohydrate Chem.*, 1951, **6**, 27.

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glucose were absent. The whole fraction (6 g.) was heated in 0·33N-sulphuric acid (550 ml.) in a boiling-water bath for 3·25 hr. The cooled hydrolysate was neutralised with 6N-sodium hydroxide and fractionated on charcoal–Celite (4·5 × 80 cm.). The column was eluted with water (1·4 l.) and then by gradient elution, 15% aqueous ethanol being fed into water (10 l.) in the mixing chamber, and 100 ml. fractions being collected. Mannose was removed by water, and chromatographically pure fraction *A* (220 mg.) was found in fractions 46—53. The next series of fractions contained fractions *C*, *D*, and a substance having $R_{mannose}$ 0·0 (fraction *E*). The substances had not been separated sufficiently well, and so fractions 55—91 were combined and 600 mg. of the total of 803 mg. were separated on thick filter paper into fractions *C* (165 mg.), *D* (130 mg.), and *E* (45 mg.). Fraction *A* had $[\alpha]_D$ +59°, *C* +69°, *D* +68°, and *E* +67·5° in water.

Periodate Oxidation of Mannan I and Mannan Oligosaccharides.—Mannan I was dissolved in water, the solution clarified by passing through a Seitz filter, and its concentration (472 mg./25 ml.) determined by acid-hydrolysis for 6 hr. with measurement of the mannose liberated. On periodate oxidation the following data were obtained (results are in moles per mannose unit):

Time (hr.)	4·25	22·75	47·5	74·75	
Periodate uptake	1·07	1·30	1·37	1·28	
Time (hr.)	5·0	18·75	28·5	42·5	65
Formic acid liberated	0·22	0·30	0·32	0·33	0·35

Fractions 87—108 (200 mg.) were dissolved in water (10 ml.), and the amount of oligosaccharide, calculated as $C_6H_{10}O_5$, was determined by acid-hydrolysis as 182 mg. When oxidised with periodate the results were as follows (moles per mannose unit):

Time (hr.)	4	8·7	23·5	49·25	71·75	95·7	—	—
Periodate uptake	1·52	1·66	1·79	1·75	1·85	1·85	—	—
Time (hr.)	4	9·5	24	33·5	47·25	72·5	119·5	143·5
Formic acid liberated	0·59	0·74	0·86	0·88	0·91	0·96	1·03	1·05

Acid-reversion of Mannose.—Mannose (36 g.) was heated in 0·33N-sulphuric acid (4 l.) for 10 hr. in a boiling-water bath. After cooling and neutralisation (sodium hydroxide), the solution was fractionated on charcoal–Celite (7 × 150 cm.). Fractions of 200 ml. each were collected, the column being eluted with water (5·2 l.), 10% ethanol (5·4 l.), and 50% ethanol (1·8 l.). Fractions 11—22 displayed positive optical rotation, and paper chromatography showed only mannose to be present. Fractions 32—44 had negative rotation and chromatography showed five sugars (*P*—*T*), that with the greatest R_F value (*P*, $R_{mannose}$ 1·50) being non-reducing. This was followed, in order of decreasing R_F value, by a trace of a reducing sugar (*Q*), mannose (*R*), and two spots (*S*, *T*) moving close to each other and in the position occupied by the α-1,6-linked dimannose (fraction *A*). The solution of fractions 32—44 was treated with barium hydroxide–zinc sulphate [28] to remove substances interfering with measurement of reducing power [15] and then diluted to 50 ml. The mannose content, determined by acid-hydrolysis, was 589 mg. (as monosaccharide). A 10-ml. portion of the solution was fractionated on thick filter paper into three zones, *P*, *Q* + *R*, and *S* + *T*, the mannose contents of which were determined by elution and acid-hydrolysis. Elution of an untreated sheet of filter paper gave no optically active material and a negligible reducing power, equivalent to 0·28 mg. of mannose per 343 sq. cm. of paper. In terms of the whole 50 ml. sample the amounts of sugar, as mannose, were *P* 366 mg., *Q* + *R* 16 mg., *S* + *T* 192 mg., a recovery of 97·4%. The yield of *P*, as 1,6-anhydromannose (see below), was 329 mg. and of *S* + *T*, as disaccharide, was 182 mg. Fraction *P* had $[\alpha]_D$ −126° in water. By fractionation of the remainder of the reversion products 177 mg. of *P* were obtained which formed a crystalline acetate (253 mg.; pyridine–acetic anhydride), m. p. 81° and $[\alpha]_D$ −121° (in $CHCl_3$). 1,6-Anhydromannose has $[\alpha]_D$ −127·6°, and its tri-*O*-acetate has m. p. 90—91° and $[\alpha]_D$ −123·6°.[28] Fraction *Q* + *R* had $[\alpha]_D$ +8·8° in water, and *S* + *T* +39·3° in water.

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[29] Knauf, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1941, **63**, 1447.

7. *Complexes between Molybdate and Acyclic Polyhydroxy-compounds.*

By E. J. Bourne, D. H. Hutson, and H. Weigel.

The compositions of complexes between molybdate and some acyclic polyhydroxy-compounds have been determined. Ionophoresis of reduced oligosaccharides in molybdate solution has been shown to be a useful method for determining the position of the glycosidic linkage to the reducing group of the original oligosaccharide.

It is known [1] that complexes of molybdate with polyhydroxy-compounds in aqueous solution have a maximum stability at acidic pH values and are decomposed by alkali. In a previous paper [2] we discussed the behaviour of sugars and other cyclic polyhydroxy-compounds, with six atoms in the ring, during ionophoresis in molybdate solution. We now report studies on the complexes between molybdate and acyclic polyhydroxy-compounds.

The effect of pH on the specific rotations of some acyclic polyhydroxy-compounds in molybdate solution was examined in order to find suitable conditions for ionophoresis. It can be seen from the results (Fig. 1) that maximal changes in specific rotation, and hence maximal complex-formation, occurred at *ca.* pH 2, but that there was some complex-formation over the whole range of pH 1—8. Ionophoresis was therefore carried out at pH 5, a value which is low enough to assure presence of sufficient complex and high enough to allow reasonable ionisation. The M_S values of acyclic polyhydroxy-compounds are shown in Table 1.

Table 1. *M_S Values of acyclic polyhydroxy-compounds.*

$$M_S = \frac{\text{true distance of migration of compound}}{\text{true distance of migration of sorbitol}}$$

Compound	M_S	Compound	M_S
Ethane-1,2-diol	<0·1	2,3-Di-*O*-methylsorbitol	<0·1
Propane-1,2-diol	<0·1	4-*O*-α-D-Glucopyranosylsorbitol	0·4
Propane-1,3-diol	<0·1	4-*O*-β-D-Glucopyranosylsorbitol	0·4
Butane-2,3-diol	<0·1	4-*O*-β-D-Galactopyranosylsorbitol	0·4
Butane-1,3-diol	<0·1	4-*O*-α-Isomaltosylsorbitol	0·4
Butane-1,4-diol	<0·1	4-*O*-α-Nigerosylsorbitol	0·4
Pentane-1,5-diol	<0·1	5-*O*-α-D-Glucopyranosylsorbitol	0·8
Hexane-1,6-diol	<0·1	6-*O*-α-D-Glucopyranosylsorbitol	0·8
2-Methylpentane-2,4-diol	<0·1	6-*O*-β-D-Glucopyranosylsorbitol	0·8
2-Methylhexane-1,3-diol	<0·1	6-*O*-α-D-Galactopyranosylsorbitol	0·8
Pentaerythritol	<0·1	6-*O*-α-Isomaltosylsorbitol	0·7
Glycerol	<0·1	6-*O*-α-Isomaltotriosylsorbitol	0·6
Erythritol	1·0	6-*O*-α-Isomaltotetraosylsorbitol	0·5
D-Threitol	0·5	6-*O*-α-Isomaltopentaosylsorbitol	0·4
Ribitol	1·1	6-*O*-α-Isomaltohexaosylsorbitol	0·3
D-Arabitol	1·1	6-*O*-α-Isomaltoheptaosylsorbitol	0·25
3-*O*-α-D-Galactopyranosyl-D-arabitol	<0·1	D-Mannitol	1·0
Xylitol	1·1	1-Deoxy-D-mannitol	1·0
Sorbitol	1·0	2-*O*-Methyl-D-mannitol	1·0
2-Deoxysorbitol	1·0	2-*O*-α-D-Glucopyranosyl-D-mannitol	0·8
2-*O*-β-D-Glucopyranosylsorbitol	0·9	2-*O*-α-D-Mannopyranosyl-D-mannitol	0·8
3-*O*-Methylsorbitol	<0·1	3-*O*-α-D-Mannopyranosyl-D-mannitol	<0·1
3-*O*-α-D-Glucopyranosylsorbitol	<0·1	1,2-Di-*O*-methyl-D-mannitol	1·0
3-*O*-β-D-Glucopyranosylsorbitol	<0·1	Galactitol	1·0
3-*O*-α-Maltosylsorbitol	<0·1	6-Deoxy-D-galactitol	1·0

[1] Gernez, *Compt. rend.*, 1891, **112**, 1360; Honnolaitre, *Ann. Chim.* (*France*), 1925, **3**, 5; Tanret, *Bull. Soc. chim. France*, 1921, **29**, 670; Richtmyer and Hudson, *J. Amer. Chem. Soc.*, 1951, **73**, 2249; Barker, Bourne, Foster, and Ward, *Nature*, 1957, **179**, 262; Rimbach and Ley, *Z. phys. Chem.*, 1922, **100**, 393; Frèrejacque, *Compt. rend.*, 1935, **200**, 1410; Sonbarew-Chatelain, *Compt. rend.*, 1939, **208**, 1652; Kaputinski, *Zhur. obshchei Khim.*, 1949, **19**, 219; Plško, *Chem. Zvesti*, 1958, **12**, 312.

[2] Bourne, Hutson, and Weigel, *J.*, 1960, 4252.

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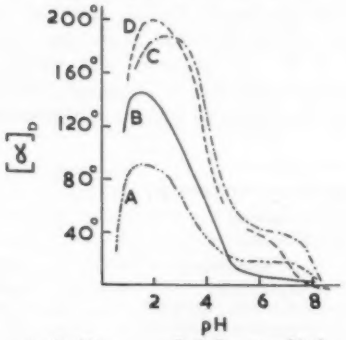
A further examination was made of the effect of the relative concentrations of the polyhydroxy-compounds and molybdate on the specific rotations of the former at pH values between 2 (Fig. 2) and 5. The rotation became constant when either one or two mol. of molybdate had been added. This revealed the compositions of the complexes which were found to be unchanged over this pH range, although the specific rotations were lower at the higher pH value. The specific rotations, when based on the polyhydroxy-compounds, were also found to be independent of the absolute concentrations of the solutions.

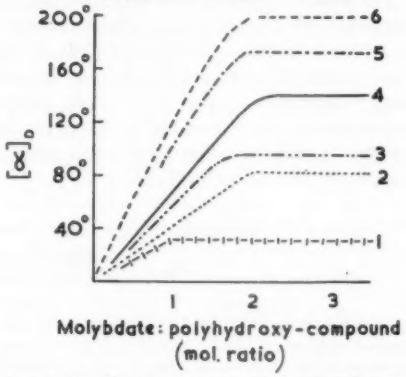
The behaviour of the complexes between polyhydroxy-compounds and molybdate during paper chromatography was examined as a possible analytical method. Impregnation of the paper with acidic molybdate solution [3] before chromatography did not yield reproducible results. When the complexes were formed by dissolving sodium molybdate and the polyhydroxy-compounds in the molar ratio of 2 : 1, and the sodium ions removed

FIG. 1. *Effect of* pH *on* $[\alpha]_D$ *of polyhydroxy-compounds in molybdate solutions (molar ratio molybdate/polyhydroxy-compound = 3).*



A, *Sorbito*. C, 2-*Deoxysorbitol*.
B, *Mannitol*. D, D-*Arabitol*.

FIG. 2. *Effect of relative concentrations of polyhydroxy-compounds and molybdate on* $[\alpha]_D$ *of polyhydroxy-compounds at* pH2.



1, 4-O-β-D-*Glucopyranosylsorbitol*. 2, 6-O-α-D-*Galactopyranosylsorbitol*. 3, *Sorbitol*. 4, D-*Mannitol*. 5, 2-*Deoxysorbitol*. 6, D-*Arabitol*.

with an ion-exchange resin, the resulting solutions could be chromatographed. Paper chromatography in acidic or neutral solvents revealed (Table 2) a trace of molybdic acid remaining on the origin line and traces of the polyhydroxy-compounds which migrated at their normal rate. In each case, between these two spots one or two components could be detected. We believe that these are mono- and di-molybdate complexes of the polyhydroxy-compounds.

The dihydroxy-compounds examined did not migrate during ionophoresis (Table 1) and hence do not form complexes with molybdate. This suggests that at least three hydroxyl groups are required for complex-formation with molybdate, as is the case for sugars and other cyclic polyhydroxy-compounds with six ring-atoms.[2] In agreement with Richardson's results,[4] glycerol did not form a complex.

It can be seen from Fig. 2 and Table 2 that sorbitol and 2-deoxysorbitol will each form a complex containing two molybdenum atoms per molecule. A 3-*O*-substituted sorbitol does not migrate during ionophoresis in molybdate solution (Table 1) and hence does not give a complex. Since the α- and β-D-glucopyranosides and D-galactose do not give a

[3] Swain, *Biochem. J.*, 1953, **53**, 200.
[4] Richardson, *J. Inorg. Nuclear Chem.*, 1959, **9**, 267.

complex,[2] it is evident that each molecule of 4-*O*-substituted sorbitol will form a complex containing one molybdenum atom, and each molecule of 6-*O*-substituted sorbitol a complex containing two molybdenum atoms (Fig. 2). As a mixture of 5-*O*-α-D-glucopyranosyl-sorbitol and 2-*O*-α-D-glucopyranosyl-D-mannitol, obtained by reduction of leucrose, migrated during ionophoresis at the same rate as 6-*O*-α-D-galactopyranosylsorbitol it is reasonable to assume that a 5-*O*-substituted sorbitol also will form a complex containing two molybdenum atoms.

D-Mannitol and D-arabitol each form a complex containing two molybdenum atoms (Fig. 2 and Table 2). 3-*O*-Substituted D-arabitol does not form a complex (Table 1). Richardson [4] has found by conductometric measurements that erythritol forms a complex containing one molybdenum atom: our chromatographic method (Table 2) has confirmed this.

It is clear that more studies are necessary before the detailed structures of the complexes between molybdate and acyclic polyhydroxy-compounds can be assigned. The problem is more difficult than in the case of cyclic polyhydroxy-compounds: *e.g.*, the number of conformations which can be adopted by an acyclic polyhydroxy-compound is very much greater. It was thought that the application of ionophoresis of polyhydroxy-compounds in molybdate solution was of greater immediate value than the assignment of the structure of the complexes.

In a previous paper [2] we reported the M_S values (defined in Table 1) of sugars and other cyclic polyhydroxy-compounds. It can now be seen that the common sugars may easily be separated from their reduction products. The method has found routine use in checking the complete reduction of sugars during treatment with sodium borohydride.

The compositions of the complexes between molybdate and substituted sorbitols suggested that the M_S values of *O*-glycosylsorbitols obtained by reduction of oligosaccharides with D-glucose as the reducing end-group would fall into three well-defined groups, *i.e.*, of those with 1,3-, 1,4-, and 1,2- or 1,5- or 1,6-glycosidic linkages.[5] This has been shown to be so (Table 1). The M_S values of the three groups of *O*-glycosylsorbitols derived from di- and tri-saccharides are $<0{\cdot}1$, $0{\cdot}4$, and $0{\cdot}7$—$0{\cdot}9$, respectively, thus allowing an efficient separation. Foster [6] has shown that disaccharides of D-glucose with 1,2- or 1,4-glucosidic linkages can be differentiated from those with 1,3- or 1,6-glucosidic linkages by ionophoresis in borate solution. Ionophoresis in molybdate solution is hence complementary to that in borate solution.

Ionophoresis in molybdate solution can be applied also to the reduction products of oligosaccharides containing up to 8 glucose units, as the M_S values are reasonably high, especially if the reducing glucose unit of the original oligosaccharide was linked by a 1,6-linkage. Table 1 shows the M_S values of the reduced oligosaccharides of the isomaltose series.

Table 1 also shows that 3-*O*-glycosyl-D-mannitol and 2-*O*-glycosyl-D-mannitol can be readily separated by ionophoresis in molybdate solution.

Experimental

Effect of pH *on Optical Rotation of Acyclic Polyhydroxy-compounds in Molybdate Solutions.*—Several solutions containing hydrated sodium molybdate and the polyhydroxy-compound (*ca.* 1—3%) in the molar ratio of 3 : 1 were adjusted with sulphuric acid to pH values between 1 and 8. The optical rotations measured were expressed as $[\alpha]_D$ and based on the polyhydroxy-compound. The results are shown graphically in Fig. 1.

Paper Ionophoresis.—Paper ionophoretograms were prepared by applying a voltage of 20—80 v per cm. across 10 cm. wide lengths of Whatman No. 3MM filter-paper for 1—2 hr. in

[5] Bourne, Hutson, and Weigel, *Chem. and Ind.*, 1959, 1047.
[6] Foster, *Adv. Carbohydrate Chem.*, 1957, **12**, 81.

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an apparatus similar to that described by Gross,[7] to whom we are grateful for advice. The electrolyte consisted of hydrated sodium molybdate (25 g.) in water (1200 ml.) adjusted to pH 5 with sulphuric acid. Compounds were detected with acetone–silver nitrate–alcoholic sodium hydroxide [8] or by spraying the paper with 0·1N-sulphuric acid and heating it at 120° for 10 min. The latter treatment caused all compounds containing primary hydroxyl groups to appear as bluish-green spots. Migration rates (Table 1) were expressed as M_S values.[2]

Effect of Relative Concentrations of Acyclic Polyhydroxy-compounds and Molybdate on the Optical Rotation of the Former.—Solutions containing the polyhydroxy-compound (*ca.* 1—14%) and hydrated sodium molybdate in varying molar ratios were adjusted to pH 2 with sulphuric acid. The optical rotations measured were expressed as $[\alpha]_D$ and based on the polyhydroxy-compound. The results are shown graphically (Fig. 2) by plotting $[\alpha]_D$ against the molar ratio of molybdate and polyhydroxy-compound. Repetition of the experiments at pH 5 resulted in lower values of $[\alpha]_D$ but no change in the shapes of the curves.

Paper Chromatography of Pre-formed Complexes between Molybdate and Acyclic Polyhydroxy-compounds.—Complexes were formed by dissolving polyhydroxy-compounds (1 mol.) and hydrated sodium molybdate (2 mol.) in water and adjusting the solutions to pH 2 with Amberlite IR-120 (H^+). The solutions were then spotted on to Whatman No. 1 filter-paper and the paper was irrigated with the organic layer of a mixture of butan-1-ol–acetic acid–water (4 : 1 : 5). Acetone–silver nitrate–alcoholic sodium hydroxide [8] was used to locate polyhydroxy-components, and an aqueous solution of catechol [9] (5%) to locate molybdate-containing components. The results are shown in Table 2.

TABLE 2.

Compound	$R_{Glucose}$	$R_{Glucose}$ of components of pre-formed complexes			
Sorbitol	1·0	0·9 *	0·6 *†	0·5 *†	0 †
2-Deoxysorbitol	1·2	1·2 *	0·7 *†	0·4 *†	0 †
D-Mannitol	1·1	0·9 *	0·7 *†	0·5 *†	0 †
Galactitol	1·1	1·1 *	0·7 *†	0·5 *†	0 †
D-Arabitol	1·1	1·1 *	0·7 *†	0·4 *†	0 †
Erythritol	1·7	1·7 *	1·2 *†		0 †
Glycerol	2·2	2·2 *			0 †
Molybdic acid					0 †

* Detected with acetone–silver nitrate–alcoholic sodium hydroxide.
† Detected with aqueous solution of catechol.

The organic phase of a mixture of butanol–ethanol–water (4 : 1 : 5) gave a wider separation of the components but the spots were less discrete.

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[7] Gross, *Chem. and Ind.*, 1959, 1219.
[8] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.
[9] Pridham, *J. Chromatog.*, 1959, **2**, 605.

8. *Arsenates. Part I. Preparative, Phase-diagram, and Other Preliminary Studies of the System Chromium(III)–Arsenic Acid.*

By G. M. Lukaszewski, J. P. Redfern, and J. E. Salmon.

The preparation of hexaquochromium(III) arsenate is described and its stability and behaviour towards heat have been investigated.

In the phase diagram of the system Cr_2O_3–As_2O_5–H_2O for the range 1—29% As_2O_5, where both solutions and solids were green, the tie-lines were either parallel or divergent. The solid material which separated had ion-exchange properties.

Ion-exchange experiments on the green solutions indicated that both cationic and anionic complexes were present.

Various workers [1] have reported the preparation of a green, non-crystalline, ill-defined chromium arsenate which dissolved in acid solutions to give emerald-green solutions of uncertain character. Early attempts to correlate the data led to diverse conclusions.[2] Simon and Baumgartel,[3-5] in a systematic study, described a violet-grey, well-defined modification, and structural studies [4,5] led them to the structure $[Cr(H_2O)_6]AsO_4,H_2O$. Mention was made of rapid conversion of the compound either alone or on contact with water into a green modification of ill-defined water content, believed from tensimetric studies [5] to be polymeric. Pyrolysis and thermogravimetric studies by Guerin and Masson [6] yielded indefinite results. Measurements of pH and cryoscopic studies [4] on the emerald-green solutions were interpreted as indicating the presence of a complex species of the type $[Cr(H_2O)_nHAsO_4]^+$.

We tried to clarify these data and to compare the present system with that of the chromium–phosphoric acid system.[7,8] Also an improved method for the preparation of the violet-grey modification is reported.

Experimental and Results

Preparation and Properties of Violet-grey Chromium Arsenate.—Simon and Baumgartel's conditions [4,5] were found to be necessary but the method was somewhat uncertain, especially for larger quantities. The presence of alkali-metal ions (from the starting material) facilitated the conversion of the violet-grey into a green form of uncertain composition, and the alkali-metal ions could not easily be removed. The following method, using ammonium arsenate, reduced these tendencies. The preparation was carried out by mixing in the order given, 100 ml. portions of each of the following solutions, previously chilled in ice: M-ammonium dihydrogen arsenate; 2M-aqueous ammonia; 96% ethyl alcohol; M-hexaquochromium nitrate. After filtration the precipitate was washed successively with ethyl alcohol and ether. Analysis of a typical batch of the freshly prepared dried salt gave: Cr_2O_3, 25·50; As_2O_5, 38·23; H_2O, 36·37 {Calc. for $[Cr(H_2O)_6]AsO_4$: Cr_2O_3, 25·42; As_2O_5, 38·43; H_2O, 36·15%}.

Freshly prepared material was heated to constant weight at various temperatures, and the losses in weight were recorded. The results are given in Table 1. The thermogravimetric studies were carried out by using a Stanton thermobalance which was programmed for a linear temperature rise from 25—900° during periods varying from 3 to 12 hr. The results for the shorter periods indicated the presence of certain hydrates. Over a period of 10 hr. the effect

[1] Schweitzer, *J. prakt. Chem.*, 1846, **39**, 269; Lefevre, *Compt. rend.*, 1890, **111**, 36; Prakash and Dube, *Z. anorg. Chem.*, 1932, **208**, 166.

[2] Dede, *Z. anorg. Chem.*, 1922, **125**, 28; Rosenheim and Thon, *Z. anorg. Chem.*, 1927, **167**, 1; Prakash *et al.*, *Allahabad Univ. Studies, Sci. Sect.*, 1932, **8**, 119; Brintzinger and Jahn, *Z. anorg. Chem.*, 1937, **230**, 416; Stalhane, Canad. P. 381,656.

[3] Simon and Baumgartel, *Holz. Roh-u-Werkstoff*, 1954, **12**, 453.

[4] Simon and Baumgartel, *Z. anorg. Chem.*, 1955, **282**, 307.

[5] Baumgartel, *Z. anorg. Chem.*, 1957, **290**, 133.

[6] Guerin and Masson, (*a*) *Bull. Soc. chim., France*, 1953, 440; (*b*) *Compt. rend.*, 1957, **245**, 429.

[7] Jameson and Salmon, *J.*, 1955, 360.

[8] Redfern and Salmon, unpublished work.

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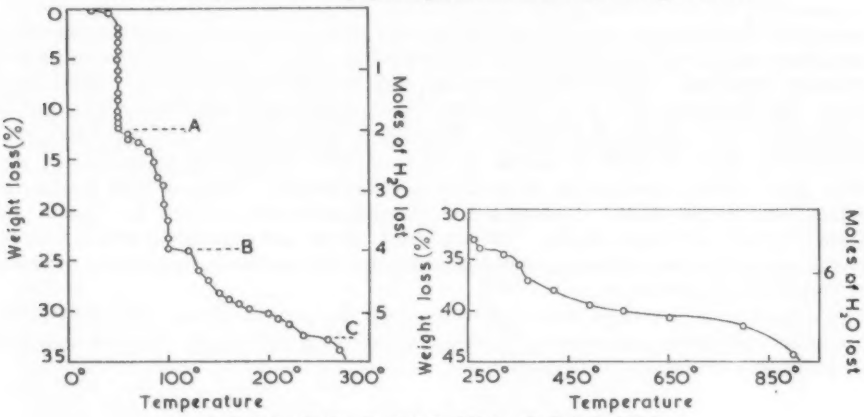
TABLE 1. *Degradation of hexaquochromium*(III) *arsenate by heating to constant weight.*

Temp. of heating	Approx. time of heating	Weight loss (%)	Mols. of H_2O lost per mol. of compound	Temp. of heating	Approx. time of heating	Weight loss (%)	Mols. of H_2O lost per mol. of compound
0°	6 months	11·95	2	320°	5 weeks	33·21	$5\frac{1}{2}$
100	1 week	23·90	4	850	4 days	41·8	6 (and some As_2O_5 (Cr_2O_3 left)
150	2 days	29·60	nearly 5	950	5 days	74·7	
180	2 days	30·07	5				

was heightened. The results (see Fig. 1) indicate the tetrahydrate to be stable up to 50°, the dihydrate up to 120°, and the hemihydrate up to 330°. Above this temperature the compound loses As_2O_5 steadily until at 950° Cr_2O_3 is the stable solid phase.

FIG. 1. *Thermobalance study of hexaquochromium arsenate during* 10 *hours.*



A, $CrAsO_4,4H_2O$; *B*, $CrAsO_4,2H_2O$; *C*, $CrAsO_4,\frac{1}{2}H_2O$.

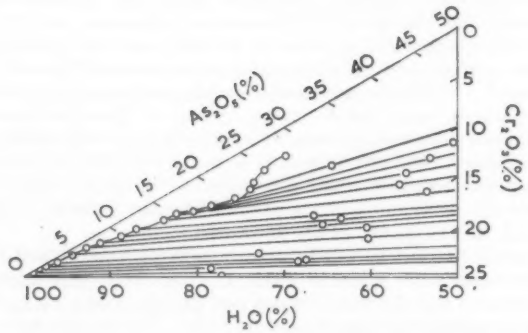


FIG. 2. Cr_2O_3–As_2O_5–H_2O *at* 25°.

Phase-diagram Studies.—The samples were contained in Pyrex boiling-tubes fitted with ground-glass stoppers and held in a lagged box in a lagged air-thermostat at 25° ± 0·1°. The solutions were prepared by dissolving the freshly prepared violet-grey chromium arsenate in solutions of arsenic acid, giving rise to an emerald-green solution immediately. In each case the arsenic acid solution was treated with small portions of the solid until no more would dissolve, then an excess of some 3—4 g. was added, and the mixture allowed to attain equilibrium during 6—8 weeks with frequent stirring. Alternate tubes in any given batch of twelve tubes were analysed at two or more weekly intervals. A smooth solubility isotherm was taken as the criterion of the attainment of equilibrium. For the range of solutions containing up to 27% of arsenic oxide no single solid phase can be isolated or identified (see Table 2 and Fig. 2). The

TABLE 2. *Phase diagram of the system chromic oxide–arsenic oxide–water at 25°.*

Solution			Solid phase		Solution			Solid phase	
Cr_2O_3 (%)	As_2O_5 (%)	pH	Cr_2O_3 (%)	As_2O_5 (%)	Cr_2O_3 (%)	As_2O_5 (%)	pH	Cr_2O_3 (%)	As_2O_5 (%)
0·10	0·60	2·20	11·25	11·40	1·68	11·20	1·71	10·60	22·80
0·15	0·95	2·08	9·85	11·65	1·90	11·83	1·48	—	—
0·20	1·78	1·97	14·10	16·95	2·50	13·70	1·50	14·80	31·70
0·25	2·30	2·00	14·45	18·15	2·54	15·05	1·30	12·25	31·00
0·28	2·55	1·96	10·65	14·42	3·37	16·35	1·52	11·60	32·50
0·41	3·36	1·91	11·10	15·90	3·72	17·80	1·50	11·55	35·35
0·46	3·85	1·95	10·75	16·40	4·41	20·00	0·90	11·25	38·40
0·57	5·05	1·68	15·72	23·75	4·35	21·85	0·85	6·50	29·05
0·78	6·45	1·74	14·70	24·75	3·92	22·60	0·42	8·45	56·80
1·05	7·60	1·70	12·05	22·50	3·23	24·60	0·14	4·95	50·60
1·50	9·60	1·65	12·30	24·30	2·89	27·10	0·04	—	—

system gave a series of parallel or diverging tie-lines similar to that encountered [9] in the system chromium(III)–phosphoric acid at 70°.

Ion-exchange Studies on the Solid obtained from the Phase-diagram Studies or from heating the Violet-grey Material at 110°.—As it was suspected that the solid material in the present system was behaving as an ion-exchanger, this possibility was further investigated. Once it had been established that the solid material isolated from the phase-diagram experiments possessed ion-exchange properties, the material used for subsequent studies was obtained by heating the violet-grey chromium arsenate at 110° for two weeks. The product, $CrAsO_4,2H_2O$, was lime-green. Weighed portions of sieved material (40—80 mesh) were loaded into small ion-exchange columns (9 × 1 cm.), back-washed to remove any adhering small particles, and washed with water. The product was not affected by water, or by acid up to 1N, even when allowed to remain in contact for some days but appeared to undergo a change in contact with dilute alkali.

Cation-exchange properties. The solid showed consistent ion-exchange properties towards H, K, Zn, and Cu^{2+} ions though very little towards Cr^{3+} itself. The results are given in Table 3.

TABLE 3. *Cation-exchange properties of green material having composition* $CrAsO_4,2H_2O$ *prepared by heating* $[Cr(H_2O)_6]AsO_4$ *at* 110° *for* 2 *weeks.*

Treatment	Behaviour
0·5N-HCl	H ions sorbed
H form with N-KCl	H ions desorbed; capacity 0·204 meq./g.
H form with 0·2N-KCl	H ions desorbed; capacity 0·192 meq./g.
H form with 0·05N-KCl	H ions desorbed; capacity 0·185 meq./g.
Zn form with N-HCl	Zn desorbed; 0·021 mmole/g.
Cu form with N-HCl	Cu desorbed; 0·018 mmole/g.
$[Cr(H_2O)_6]^{3+}$ form with N-HCl	Negligible desorption, *i.e.*, Cr not sorbed

The amount used in each experiment was approximately 1 g.; Cu and Zn forms were prepared by passage of 0·1N-sulphate solution through column. Sorption of Cu and Zn occurred with release of hydrogen ions. Metal estimated by standard EDTA solution.

Anion-exchange properties. The solid showed no anion-exchange properties either when fresh or after treatment with hydrochloric acid. No uptake of Cl^-, AsO_4^{3-}, or NO_3^- could be detected. However, treatment with 0·1N-alkali resulted in the uptake of hydroxyl ions and the release of arsenate ions which appeared to be reversible, or at least partly so. Passage of an arsenate solution resulted in a partial reversal of the process.

Batch Equilibrium Studies with Chromium Form of a Strong Cation-exchanger.—The amounts of metal removed from freshly prepared $[Cr(H_2O)_6]^{3+}$ form of ZeoKarb 225 (50—100 mesh) by arsenic, phosphoric, and perchloric acid after 7 days at 25° are shown in Fig. 3. The results indicate that complex-formation occurs between hexaquochromium(III) and arsenate ions in this time (cf. $[Cr(H_2O_6]^{3+}$–phosphate; [9] see also ref. 9 for a discussion of the method).

Uptake of Chromium and Arsenate on Cation- and Anion-exchangers from Solutions at 25°.—In these experiments 1·00 g. of De-Acidite FF in the arsenate form or 0·50 g. of ZeoKarb 225 in the hydrogen form was added to various solutions containing green chromium arsenates. After 14 days the chromium and arsenate contents of the resins were estimated after elution with

[9] Genge and Salmon, *J.*, 1957, 256.

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6N-hydrochloric acid (cf. ref. 10). The results (see Table 4) show that in both cases chromium and arsenate were sorbed to a significant extent, indicating the presence of cationic and anionic complexes in the solutions.

Analytical Methods.—Chromium was determined, after oxidation to dichromate, by addition of an excess of standard ferrous ammonium sulphate solution followed by the back-titration of the excess by potassium dichromate. Chloride ions were shown not to interfere. Arsenate

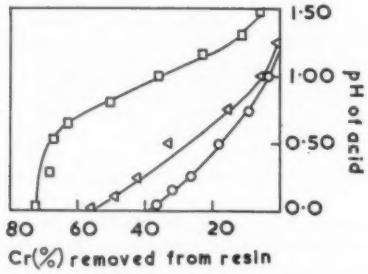

FIG. 3. *Removal of chromium from ZeoKarb 225 by various acids at 25°.*
□, H_3AsO_4; △, H_3PO_4; ○, $HClO_4$.

was determined after reduction to arsenite by using a saturated solution of sulphur dioxide (and subsequent boiling off of the excess) by titration with potassium bromate, with α-naphthaflavone as reversible bromometric indicator.[11]

DISCUSSION

The violet-grey material presumably must be formulated as $[Cr(H_2O)_6]AsO_4$ and be similar to that prepared by Simon and Baumgartel [4] except that the different conditions employed mean that the last molecule of water which these workers found is absent from our material. This may account for the increased stability of our compound. From the results obtained on heating the freshly prepared substance, it is not yet possible to ascribe a definite structure to those hydrates which are stable at the temperatures indicated. The relative ease of loss of water from the hexahydrate is of interest. Plane and Taube,[12] in studies of the kinetics of the system $[Cr(H_2O)_6]^{3+}$–H_2O, noted that the provision of an anion in which electron transfer is possible greatly accelerated the rate of exchange of bound aquo-groups and presumably also of entrance of a charged ligand group into the co-ordination sphere of the molecule. Also there is the observation that there is rapid conversion of the solid violet-grey material into a green compound on contact with water, and that it is impossible to obtain a purple solution by dissolving the hexaquo-arsenate in arsenic acid. These facts are in direct contrast to those on the otherwise similar system chromium–phosphoric acid in which electron transfer does not appear to be possible.

It has been explained elsewhere [8] that the system of parallel tie-lines observed in some phase-diagram studies could be accounted for on the assumption that the solid phase was acting as an ion-exchange material. The appearance of a similar series in the present system, coupled with the observation that the green solid from the phase-diagram experiments or the solid obtained from heating the hexaquo-arsenate behaved as a weakly acidic cation-exchanger, seems to be reasonable proof of the assumption. The behaviour with sodium hydroxide may be accounted for by replacement of some of the arsenate bridges by hydroxyl bridges with the release of arsenate ions, if the material is assumed to possess a bridged polynuclear structure.

The results obtained from the preliminary batch experiments indicate that complex formation has taken place in solution, with formation of both anionic and cationic complexes in significant amount (Table 4).

[10] Jameson and Salmon, *J.*, 1954, 4013.
[11] Tomicek, "Chemical Indicators," Butterworths, London, 1st edn., 1951, p. 543.
[12] Plane and Taube, *J. Phys. Chem.*, 1952, **56**, 33.

TABLE 4. *Uptake of chromium and arsenate by ZeoKarb 225 and DeAcidite FF from green solutions obtained by dissolving* $[Cr(H_2O)_6]AsO_4$ *in arsenic acid.*

Content of solution (mmole/ml.)				Found on resin	
Cr(III)	AsO_4	Resin form	Capacity (meq./g.)	Cr(III)	AsO_4
				mole/equiv.	
0·530	1·190	ZeoKarb 225(H)	4·17	0·577	0·565
0·127	1·950	,, ,,	2·99	0·233	0·213
0·139	0·154	DeAcidite FF(Cl)	2·89	0·071	0·137
0·270	0·008	,, (Cl)	2·90	0·060	0·158

Grateful acknowledgment is made to the Permutit Company Ltd. for a grant (to G. M. L.) and to Dr. S. P. Datta, of University College, London, for placing the thermobalance at our disposal and for helpful discussion on the heating studies.

BATTERSEA COLLEGE OF TECHNOLOGY, LONDON, S.W.11. [*Received, March 1st,* 1960.]

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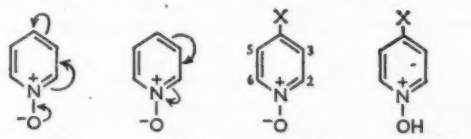
9. N-*Oxides and Related Compounds. Part XVIII.*[1] *Proton Nuclear Magnetic Resonance Spectra of* 4-*Substituted Pyridines and Pyridine* 1-*Oxides.*

By A. R. KATRITZKY and (MRS.) J. M. LAGOWSKI.

Nuclear magnetic resonance spectra of 4-substituted pyridines and pyridine 1-oxides as neutral molecules and cations are recorded and compared with those of the corresponding benzene derivatives. The data indicate that the electron density at the various ring positions decreases in the order $C_6H_6 > 3Py^* > 3PyO > 2Py > 2PyO >$ cationic rings, in agreement with other evidence.

THE pyridine 1-oxide molecule is of interest in that the NO group can act as either an electron-donor or an electron-acceptor (I, II). In previous papers in this series the importance of both types of electron drift was shown by means of dipole moment [2] and infrared- [3] and ultraviolet-spectral data.[4] These findings and chemical evidence [5] indicate



(I) (II) (III) (IV)

that the *N*-oxide group can be polarised in both directions by strongly interacting substituents or reagents. Nuclear magnetic spectra have now been used to indicate the relative electron densities at the 2- and the 3-position of pyridines and pyridine 1-oxides when these positions are unsubstituted and are not subject to the perturbing effect of an approaching reagent. 4-Substituted compounds were selected because their spectra were expected to be much simpler to interpret. Protons in the 2- and the 6-position, and those in the 3- and the 5-position (cf. III), are in identical environments, and each signal is split into a doublet by the adjacent proton. Additional splitting by diagonal coupling

* Throughout this paper Py = pyridine, PyO = pyridine 1-oxide and the preceding numeral indicates the ring position in question.

[1] Part XVII, Jones and Katritzky, *J.*, 1960, 2937.
[2] Part IV, Katritzky, Randall, and Sutton, *J.*, 1957, 1769.
[3] Part XII, Katritzky, Monro, Beard, Dearnaley, and Earl, *J.*, 1958, 2182.
[4] Part XV, Katritzky, Monro, and Beard, *ibid.*, p. 3721.
[5] Katritzky, *Quart. Rev.*, 1956, **10**, 395.

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was negligible under the conditions used. Thus, the expected pattern for the ring protons of the compounds was two doublets (Fig. 1), the intensities of the inner components of which would be increased if they lay close together (Fig. 2).

FIG. 1.

FIG. 2.

Series of 4-substituted pyridine 1-oxides and pyridines were measured in water and in 20N-sulphuric acid (*ca.* 10% w/w) to obtain the spectra of the neutral species and the cations (IV). The expected patterns for the ring protons were obtained; the doublets at the lower values were assigned to the α-protons because (i) these protons are nearer to the electron-withdrawing nitrogen atom and (ii) the position of the lower doublets depends less on the substituent (the substituent's influence should be most pronounced on the protons adjacent to it). The positions of the resonance peaks are given in the Table as chemical shifts (σ) measured in parts per million relative to water. These positions were taken as the centres of the doublets provided these centres were separated by at least 0·8 chemical shift; otherwise the standard correction was applied.[6] Water and 20N-aqueous

Chemical shifts of nuclear protons (parts per million).

		α-Protons					β-Protons				
Subst.	*meta*-Protons Benzene [a]	Pyridine	Pyridine 1-oxide	$\overset{+}{>}$N–H	$\overset{+}{>}$N–OH	*ortho*-Protons Benzene [a]	Pyridine	Pyridine 1-oxide	$\overset{+}{>}$N–H	$\overset{+}{>}$N–OH
NMe_2	−1·60	−3·08	−2·96	−3·28	−3·54	−1·30	−1·49	−1·73	−2·16	−2·21
NH_2	−1·67	−3·10	−2·93	−3·46	−3·65	−1·03	−1·72	−1·78	−2·39	−2·39
OMe	−1·57	−3·30	−3·34	−4·04	—	−1·57	−1·86	−2·30	−2·99	—
Me	−1·7	—	−3·33	—	−3·81	−1·7	—	−2·55	—	−3·10
Et	−1·73	−3·25 [b]	—	−4·04	—	−1·73	−1·80 [b,c]	—	−3·45	—
$CH_2{\cdot}OH$ ...	−1·73	−3·47	—	(—)	—	−1·73	−2·39	—	−3·65	—
Cl	−1·8	—	−3·46	—	−3·83	−1·8	—	−2·81	—	−2·88
Br	−1·8	—	−3·37	—	−3·76	−1·8	—	−2·97	—	−3·55
CN	−2·1	−3·56	—	(—)	—	−2·1	−3·04	—	−3·92	—
CO_2^-	—	−3·57	−3·49	—	—	—	−2·78	−3·05	—	—
CO_2H ...	−1·9	—	—	(—)	(—)	−2·43	—	—	−3·70	−3·91
CO_2Me ...	−2·00	−3·63	−3·57	(—)	(—)	−2·73	−2·73	−3·23	*ca.* −3·70	*ca.* −4·0
COMe ...	−2·07	−3·01 [c]	−3·57	(—)	(—)	−2·43	−2·51 [c]	−3·23	(—)	−3·85
NO_2	−2·1	—	−3·67 [d]	—	(—)	−2·77	—	−3·67 [d]	—	(—)

[a] From Ref. 7. [b] Measured in cyclohexane. [c] Doublet not resolved. [d] α- and β-Proton signals superimposed. — Compound not measured. (—) Peaks hidden by sulphuric acid signal.

sulphuric acid showed peaks at 5·22 and 9·60 p.p.m. to lower field, respectively, compared with an external tetramethylsilane reference. Dissolving *ca.* 10% w/w (*i.e.*, *ca.* $\frac{1}{60}$ mole fraction) of substituted pyridine and pyridine 1-oxides in these solvents did not appreciably alter these resonance positions (±0·02 chemical shift), and calculation showed that the difference in molar susceptibility of the solvent and solutions was negligible.* Hence, resonance peaks were measured from the solvent peaks.

In any one compound the splitting of the individual doublets should be identical for the α- and the β-protons; this was usually the case to 1 c./sec. No simple relation was

* The volume susceptibility of sulphuric acid is −0·808, and that of water is −0·721 (ref. 6, p. 488); 20N-sulphuric acid contains *ca.* 50% of H_2SO_4 by volume. Therefore values in sulphuric acid should be corrected by *ca.* $\frac{2\pi}{3} \times 0{\cdot}04 \approx 0{\cdot}08$ p.p.m., for comparison with water values; however, this has not been done.

[6] Pople, Bernstein, and Schneider, "High-Resolution Nuclear Magnetic Resonance Spectroscopy," McGraw Hill, New York, 1959, p. 122.

apparent between the degree of splitting of the doublets and the molecular structure; the mean and the standard deviation for the coupling constants were 6·4 ± 1·6 c./sec. The Table also gives values for the *ortho*- and *meta*-hydrogen resonances for monosubstituted benzenes; * [7] the *o*-values correspond to the β-protons in the heterocyclic compounds (both adjacent to the substituent) and the *m*-values to the α-protons.

Chemical Shifts of α-Protons.—The effects of the substituents and of the hetero-groups can be distinguished clearly. In each series, as the substituent is varied from a strong electron-donor (*e.g.*, NMe_2, NH_2) to a strong electron-acceptor (*e.g.*, COMe, NO_2) the peaks become more negative, the total alteration in each case being about 0·5σ.

For the same substituent, the chemical shift decreased in the order: Ph ⩾ PyO > Py ⩾ PyH^+ ~ $PyOH^+$. Although differences in ring currents for the various rings may complicate the picture, this order is consistent with the conclusion that the electron-density at the α-position is much less for all the hetercyclic compounds than for their benzenoid analogues. The differences between the pyridines and pyridine 1-oxides are small but may indicate that electron shifts of type (I) are slightly greater than the increased electron pull towards the positively charged nitrogen of the *N*-oxide, as compared with that of the corresponding pyridine. The cationic rings are very deficient in electrons at the α-positions, as would be expected.

Chemical Shifts of β-Protons.—Again, for each ring system, a reasonably steady change towards more negative values occurs as the substituent type is varied from electron-donor to electron-acceptor, but here the total change is *ca.* 1·5σ. The substituent evidently has a much greater effect on the adjacent β-protons than on the α-protons. The influence of the heterocyclic group is correspondingly less and is more difficult to separate from that of the substituents than in the case of the α-protons. For a given substituent, the chemical shift decreased in the approximate order: Ph > Py > PyO > PyH^+ ~ $PyOH^+$. With the same reservations with respect to ring currents, this order indicates that the electron density at the β-position of pyridines is lower than for benzenes, and that for pyridine 1-oxides, and especially for the cationic rings, it is lower still.

General Conclusions.—The finding that the electron density varies in the order Ph > 3Py > 3PyO > 2Py ≈ 2PyO > cationic rings for a given substituent is in good agreement with other physical and chemical data.[3,4,8] However, this order is not in accord with calculated values [9,10] for the charge distribution in pyridine 1-oxide, which suggests that the electron density should be greater at the α- than at the β-positions.

Experimental.—Compounds were recrystallised or redistilled immediately before measurement and had m. p.s or b. p.s in agreement with values in the literature.

Nuclear magnetic resonance spectra of hydrogen nuclei were obtained at 40 Mc. using a Varian Associates 4300 B spectrometer and 12″ electromagnet with flux stabilisation and sample spinning.

Addendum (July 20th, 1960). We have made further measurements which support the assignments quoted above. Formulæ (V—VIII) show resonance positions for methylpyridines which clearly support the assignments for 4-ethylpyridine (IX). Similarly, (X) and (XI) support (XII).

Measurements with compounds containing strongly interacting groups have also been made (XIII, XV, XVII, and XIX) which, on comparison with (XIV), (XVI), (XVIII),

* Values in ref. 7 are given with reference to benzene and were obtained by measuring 50% solutions in cyclohexane, using the solvent peak as standard, and adding 5·73 chemical shifts to the value obtained. To convert to water as a standard we have now subtracted 1·8 chemical shifts from each value; susceptibility variations have been neglected.

[7] Corio and Dailey, *J. Amer. Chem. Soc.*, 1956, **78**, 3043.
[8] Cf. Katritzky and Lagowski, "Heterocyclic Chemistry," Methuen, London, 1960.
[9] Jaffé, *J. Amer. Chem. Soc.*, 1954, **76**, 3527.
[10] Barnes, *J. Amer. Chem. Soc.*, 1959, **81**, 1935.

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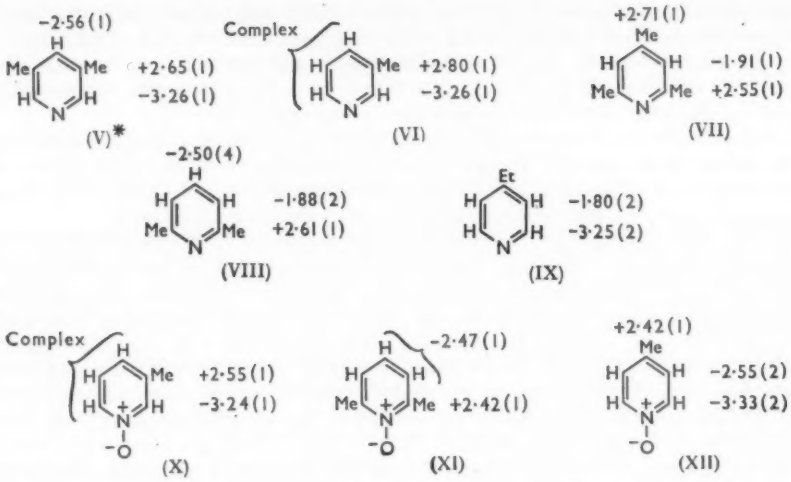
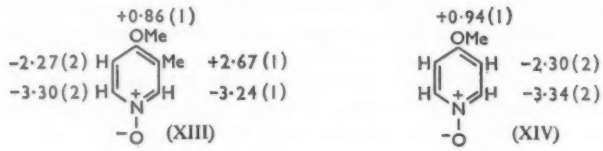
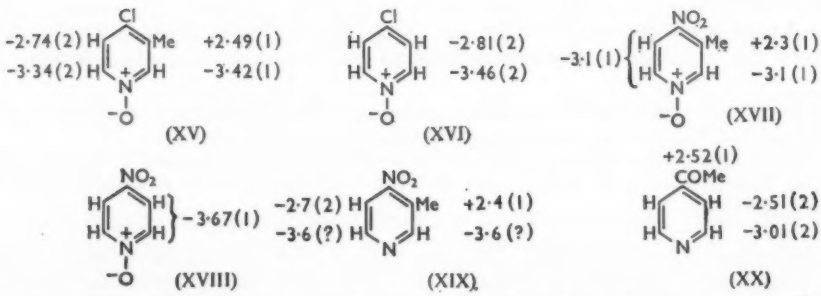


and (XX) respectively, demonstrate that there is no cross-over in the position of the bands of the protons in the 2-* and the 3-positions for the heterocyclic compounds.





It is of interest that these measurements also indicate that, whereas for pyridine the electron density of the ring positions increases $2 < 4 < 3$, for pyridine 1-oxide it is $2 < 3 \sim 4$; this is in good agreement with other evidence.[3,4,8]

We thank Dr. N. Sheppard for reading this paper in manuscript, the Wellcome Foundation for provision of the spectrometer, the Referees for very helpful comment, and Mr. Richard A. Y. Jones, B.A., M.S., for the experimental work mentioned in the addendum.

* Figures in parentheses denote multiplicity of peaks. All measurements refer to water solutions, except (XVII) in $CDCl_3$ and (XIX) in CCl_4 where measurements were made relative to an internal standard of t-butyl alcohol.

The University Chemical Laboratory, Cambridge. [*Received, May 2nd,* 1960.]

10. *A Kinetic Study of the Hydrolysis of Certain Alkyl Acetates and Corresponding Lactones.*

By J. Grace and M. C. R. Symons.

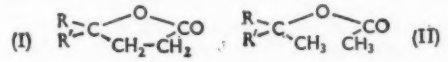
Arrhenius parameters for the alkaline hydrolysis of the esters RR′MeC·OAc where R and R′ are H, Me, or Ph are compared with those for correspondingly substituted γ-lactones. Marked differences found for highly substituted compounds are explained as steric effects. No similar comparison can be made for acid-catalysed hydrolyses because most of the γ-lactones are not hydrolysed appreciably. Optically active γ-phenyl-γ-valerolactone is readily racemised in weakly acidic media, a weak absorption band with a maximum at 520 mμ slowly developing. These phenomena are discussed.

The considerable attention that has been given to the effect of alkyl substitution on the rates of hydrolysis of esters has been directed primarily towards variations in the acid residue.[1] Taft tried to differentiate between inductive, steric, and resonance effects by using a variety of correlations [2] and suggested that in the alkaline hydrolysis of certain acetates ROAc the rates are largely independent of steric influences, variations being governed by the electronegativity of the group R.

However, for esters substituted in the β-position of the acid residue, Newman concluded that polar effects are insignificant compared with steric effects.[3] In contrast, Sarel, Tsai, and Newman [4] considered that both polar and steric effects significantly modify the rates of alkaline hydrolysis of esters when the alkyl group is changed from primary to secondary or tertiary.

Stevens and Tarbell [5] made some general observations on the marked differences in rates of base-catalysed hydrolysis of certain esters and γ-lactones, but did not differentiate between energy and entropy factors.

We have attempted to distinguish between possible contributions from polar and steric factors by comparing Arrhenius parameters for the alkaline hydrolysis of various γ-sub-



stituted γ-lactones (I) and the corresponding esters (II). If polar effects predominate, then there should be little difference in the trends for these two classes, but if steric effects are important a considerable difference is to be expected.

The results in 43% aqueous acetone are summarised in Figs. 1—3, giving bimolecular rate constants at 20° and the Arrhenius parameters log A and E, respectively, plotted against the nature of the groups R and R′ as ordinates.

The effect of increasing substitution on the rate is qualitatively similar for lactones and esters. However, the trends in log A and E for the last two members of the series are reversed, and it is this contrast with which we will primarily be concerned.

Kinetic Form of Alkaline Hydrolysis.—A second-order rate law was obeyed, as required for mechanism $B_{AC}2$. In accord with this was the complete retention of activity when (−)-γ-phenyl-γ-valerolactone was re-formed after alkaline hydrolysis.

It seemed possible that some of the differences (Figs. 1—3) could arise because of a change in reaction from hydrolysis to elimination. However, the ultraviolet and infrared

[1] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953.
[2] Taft in " Steric Effects in Organic Chemistry," ed. Newman, John Wiley and Sons, Inc., New York, 1956, p. 556.
[3] Newman, see ref. 2, p. 201.
[4] Sarel, Tsai, and Newman, *J. Amer. Chem. Soc.*, 1956, **78**, 5387.
[5] Stevens and Tarbell, *J. Org. Chem.*, 1954, **19**, 1996.

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spectra of the products obtained by hydrolysis of the phenyl-substituted compounds showed that olefins had been formed, if at all, in negligible amounts.

Intermediates.—Bender [6] established that an intermediate of life-time sufficiently great to permit proton migration is formed during alkaline hydrolysis of a series of benzoates, including t-butyl benzoate. The only reasonable structure for this intermediate is one in which the trigonally hybridised carbonyl-carbon atom has become tetrahedral, and extrapolation from the benzoates to the esters and lactones now discussed seems reasonable. Since the rate of ^{18}O exchange was somewhat less than the rate of hydrolysis, and since

FIG. 1. *Variations in second-order rate constants (k) for the alkaline hydrolysis of esters (E) and γ-lactones (L) in 43% (w/w) aqueous acetone at 20°. The ordinate gives the groups R and R′ for the esters and corresponding lactones. HHH refers to methyl acetate.*

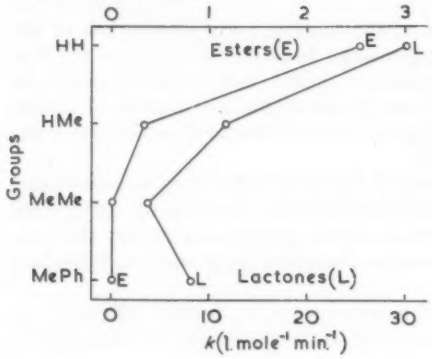
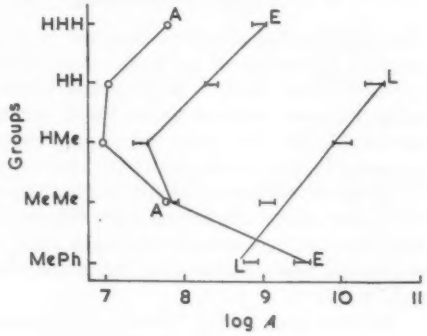


FIG. 2. *Variations in* log *A for the alkaline hydrolysis of esters (E) and γ-lactones (L), and for the esterification of certain β-substituted carboxylic acids (A).*[10]



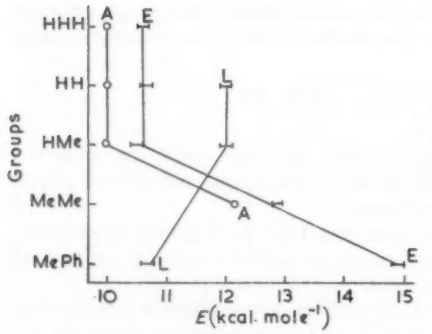


FIG. 3. *Variations in activation energy for the alkaline hydrolysis of esters (E) and γ-lactones (L), and for the esterification of β-substituted carboxylic acids (A).*[10]

proton exchange in the complex should be rapid, the energy barriers enclosing the complex must be small, relative to the overall barrier to reaction, and the transition states for the loss of this complex probably resemble the complex more closely than they resemble the reactants or products.

The results can be discussed in terms of two alternative transition states: that in which the bond between hydroxyl-oxygen and carbonyl-carbon atom has not completely formed, and that in which the bond between alkoxyl-oxygen and carbonyl-carbon atom has begun to break. Since the intermediate has never been detected by direct physical means, we infer that its concentration must be small at all times and that stationary-state kinetics may therefore be used.

[6] Bender, *J. Amer. Chem. Soc.*, 1951, **73**, 1626.

This gives the following expression for the overall rate of hydrolysis:

$$\text{Rate} = \frac{k_1 k_2}{k_{-1} + k_2}\,[\text{OH}^-][\text{Ester}]$$

where k_1, k_{-1}, and k_2 are the rate constants for the individual steps:

$$\text{ROAc} + \text{OH}^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{Complex}$$

$$\text{Complex} \xrightarrow{k_2} \text{Products}$$

Hence the overall rate constant, k', found experimentally is given by:

$$k' = k_1 k_2/(k_{-1} + k_2)$$

If we set $k_{-1} = xk_2$, this may be written $k' = k_1/(x + 1)$. Making the postulate that the rates of proton exchange in all the intermediate complexes considered here are nearly equal, one can conclude that x is approximately constant, since the ratio of ^{18}O exchange to hydrolysis, reported by Bender, is remarkably similar for all esters,[6] and hence to a first approximation the rate constants can be discussed in terms of the transition state for the formation of the intermediate complex.

The following is based upon this approximation.

Effect of Substituents.—Trends in the Arrhenius parameters for the hydrolysis of esters and corresponding lactones on substitution are similar for esters of primary and secondary alcohols, but change abruptly for esters of tertiary alcohols, in contrast to the lactones (Figs. 1—3).

These changes could be due to polar, resonance, or steric interactions. Even in the phenyl-substituted compounds it is hard to see how any resonance effect could play a significant rôle. It has, however, been suggested that polar effects should be important.[2] Such effects should be comparable for esters and γ-lactones, so the differences must be caused by some other, over-riding phenomenon. For various reasons, it seems to us that polar effects will be unimportant for this class of esters. (i) Substitution in the α-position of the alkyl group is equivalent to β-substitution in the acid residue, and the latter is thought to have only a small polar effect.[3] (ii) Electron-release to carbonyl-carbon and -oxygen atoms would alter the energy term, leaving the pre-exponential factor unchanged: this is the reverse of what is found for esters of primary and secondary alcohols. (iii) The effect of a methyl should be opposite to that of a phenyl group: in fact, when methyl is replaced by phenyl the trend ascribed to methyl is enhanced. (iv) The rate of alkaline hydrolysis of diphenylmethyl acetate [7] is practically unchanged when phenyl is replaced by *p*-methoxyphenyl.[8] These considerations lend weight to the suggestion that the significant step involves formation rather than decomposition of the intermediate complex.

It is therefore concluded that the trends reported above are primarily due to steric interactions in the transition state.

Entropy of Activation.—The small, steady decrease in $\log_{10} A$ for all the lactones and for esters of primary and secondary alcohols is probably due to steric and ponderal effects [9] (cf. Fig. 2); it does not seem to be related to changes in the energy of activation since these changes are negligibly small except for esters of tertiary alcohols.

A study of scale models shows that for esters of tertiary alcohols, but not others, the only strain-free conformation is one in which the molecule is coiled so that one side of the plane of the carbonyl group is quite open, the methyl groups being pressed close to the carbonyl-carbon atom on the other side. Thus approach of hydroxide ion on one side is

[7] Israel, unpublished results quoted in ref. 8.
[8] Bunton and Hardwick, *J.*, 1957, 3043.
[9] Ingold, *Quart. Rev.*, 1957, **11**, 1.

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probably completely prevented whereas a very wide angle of approach is available on the other. This situation does not arise for any of the lactones, and we postulate that the sudden change in the trends for esters of tertiary alcohols is due to coiling.

Energy of Activation.—As the C–OH bond begins to form, the carbonyl-carbon atom must change its hybridisation from sp^2 to sp^3 and hence the carbonyl-oxygen atom must be forced against the coiled chain in esters of tertiary alcohols. This should lead to a major increase in the energy of activation (cf. Fig. 3). At the same time, the intermediate complex will be destabilised because of crowding, but this should be less marked than the effect on the transition state. If that is so, then the transition state may resemble the intermediate complex less in the crowded esters: this would then lead to an increase in entropy of activation (cf. Fig. 2).

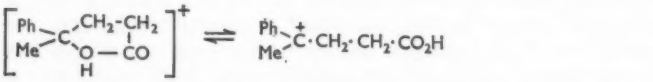
It is possible to understand the trends shown in the Figures in terms of a change in mechanism from one involving a stable addition complex to a direct S_N2 displacement. However, Bender [6] found appreciable oxygen exchange during the hydrolysis of esters of tertiary alcohols so this simple explanation is untenable.

Comparison with Other Data.—There is a striking resemblance between the results presented in Figs. 1—3 for esters of primary, secondary, and tertiary alcohols and those for esterification of acids substituted on the β-carbon atom.[10] These results, summarised in Figs. 2 and 3, strongly support the earlier suggestion that the substitutions effected here resemble substitutions on β-carbon in the acid. We suggest that the reasoning given above to explain the present results applies equally to the data of Newman's school.[10]

Emphasis has been on the different trends in the Arrhenius parameters with increasing substitution for esters and γ-lactones. The fact that γ-lactones are hydrolysed by alkali more readily than corresponding esters has been discussed by Huisgen and Ott,[11] who consider an important factor to be that γ-lactones are constrained into a *cis*-configuration with respect to the carbonyl group, whereas open esters normally have a *trans*-configuration. Our results show that, for γ-lactones, the high rate is a result of a more favourable entropy of activation. This is thought to be, in part, because esters have far more motional freedom to lose on going to the transition state than have the corresponding actones.

Acid-catalysed Hydrolysis.—Since acids catalyse the lactonisation of γ-hydroxy-acids the comparison made for alkaline hydrolyses could not be extended to cover acid-catalysed hydrolyses.

The acid-catalysed racemisation of γ-phenyl-γ-valerolactone is most simply understood in terms of the transient formation of a planar carbonium ion after protonation:



It was at first though that a very weak band at 520 mμ developing slowly in acid solutions of this lactone might have been due to this carbonium ion. However, in the light of subsequent work on the spectra of monoarylcarbonium ions in concentrated sulphuric acid,[12] this conclusion seems most improbable since the comparable ion $PhMe_2C^+$ was found [12] to have an intense band with a maximum at 390 mμ.

In concentrated sulphuric acid γ-phenyl-γ-valerolactone also gives a yellow solution, with a band at about 360 mμ. This we tentatively ascribe to the carbonium ion (possibly also protonated on the carbonyl group). The appearance of a pink colour in weakly acidic solutions is reminiscent of the behaviour of several other compounds, and a discussion given elsewhere may be relevant.[12] The only significant additional information that this result provides is that racemisation is faster than development of colour. Hence the

[10] Loening, Garrett, and Newman, *J. Amer. Chem. Soc.*, 1952, **74**, 3929.
[11] Huisgen and Ott, *Tetrahedron*, 1959, **6**, 253.
[12] Grace and Symons, *J.*, 1959, 958.

planar carbonium ion may well be an essential intermediate in the formation of the coloured species.

Experimental

Materials.—γ-Phenyl-γ-valerolactone, prepared from ethyl lævulate and bromobenzene,[13] had b. p. 89—92°/0·04 mm. The lactone was converted into γ-hydroxy-γ-phenylvaleric acid which was resolved as its brucine salt.[14] The resulting optically active acid was lactonised by azeotropic distillation with dry benzene, since it is readily racemised in acid solution.

t-Butyl acetate, prepared from t-butyl alcohol and acetyl chloride, in the presence of dimethylaniline, had b. p. 97—98°.

Phenylpropan-2-ol, prepared from acetone and phenylmagnesium bromide, had b. p. 52°/3 mm. This, with acetyl chloride and dimethylaniline in ether, gave the acetate, b. p. 58—61°/3 mm.

Other reactants and solvents were dried and purified by standard procedures.

Carbonate-free solutions of potassium hydroxide in water, aqueous acetone, and aqueous dioxan were prepared in an atmosphere of carbon dioxide-free nitrogen in a dry-box. Sticks of "AnalaR" grade potassium hydroxide were liberally washed with water to remove carbonates before being dissolved in purified water, the resulting solutions being stored in bottles coated internally with wax to prevent the formation of soluble silicates. These solutions were standardised against potassium hydrogen phthalate, with standard procedures to prevent access of atmospheric carbon dioxide. The calculated quantity of purified acetone or dioxan was added to the standardised solutions. Since acetone reacts slowly with potassium hydroxide, solutions were used immediately after preparation. Solutions of lactones were prepared in the same solvent mixtures, and reaction was initiated by rapid mixing in a two-limbed stoppered tube after temperature equilibration.

Method.—The reactions were followed titrimetrically by quenching aliquot parts with excesss of standardised hydrochloric acid followed by back-titration under carbon dioxide-free conditions. Hydrolysis of optically active γ-phenyl-γ-valerolactone was also followed polarimetrically, a polarimeter tube controlled within 0·05° being used. For low-temperature studies, jets of dry nitrogen were directed on the end-plates of the tube to prevent misting. For each reaction at least three temperatures were selected, and reactions were followed to more than 80% completion, the course being accurately of second-order under all conditions. In most cases the initial concentrations, a, of the reactants were equal, and the second-order rate constant k was estimated from plots of time, t, against $(a - x)^{-1}$.

Arrhenius parameters for the alkaline hydrolysis of certain esters and lactones in aqueous acetone.

	R	R′	Acetone (% w/w)	E (kcal./mole)	log A	k (l. mole^{-1} min.$^{-1}$, 20°)	Ref.
Esters	H	H	43	10·70	8·38		*b*
	H	H	62	12·0	9·2		*c*
	H	Me	43	10·53	7·43	0·3548	*a*
	H	Me	62	12·20	8·5		*c*
	Me	Me	43	12·9	7·85	0·0171	*a*
	Me	Me	62	14·3	8·7		*c*
	Me	Ph	43	14·92	9·5	0·0233	*a*
	Me	Ph	62	16·78	10·42	0·0099	*a*
	(AcOMe)		43	10·60	8·94	10·71	*a*
	"		62	12·0	9·2	9·2	*c*
Lactones	H	H	43	12·0	10·4		*b*
	H	Me	43	12·3	10·2		*b*
				12·0	10·0		*d*
			62	13·2	10·8		*d*
	Me	Me	43	11·4	9·07		*b*
	Me	Ph	43	10·7	8·86	8·18	*a*
	Me	Ph	62	12·06	9·9	7·50	*a*

Refs.: *a*, This work. *b*, Tommila, Koivisto, Lyyra, Antell, and Heimo, *Ann. Acad. Sci. Fennicae*, 1952, **47**, *A*, 3. *c*, Raylander and Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 3021. *d*, Tommila and Ilomaki, *Acta Chem. Scand.*, 1952, **6**, 1249.

[13] Kenyon and Symons, *J.*, 1953, 2129.
[14] Kenyon and Symons, *J.*, 1953, 3580.

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The results, together with those obtained by others, are summarised in the Table. Some selected results are displayed in the Figures, in order to summarise the important trends and differences for esters and γ-lactones.

Racemisation of (−)-γ-Phenyl-γ-valerolactone.—Solutions in acetic acid were stable at room temperature. Adding a trace of sulphuric acid caused rapid racemisation according to a first-order rate law. In more acidic solutions, racemisation was too fast to be followed kinetically, so no attempt was made to measure rate as a function of acidity. Several hours after racemisation was complete a pink colour was detected in these solutions, and spectral analysis revealed a weak band at 520 mμ. The final intensity of this band increased with increasing acidity, reaching a maximum in the 30% sulphuric acid region. At all acidities the rate of growth was far less than the rate of racemisation. In 100% sulphuric acid no band at 520 mμ could be detected, but there was an intense band at 360 mμ ($\varepsilon_{max.} \approx 10^4$). At intermediate acidities both bands were found.

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11. *The Formation of Melanin from Adrenochrome.*

By JOHN D. BU'LOCK.

The non-oxidative transformation of adrenochrome into melanins in acid solution is controlled in rate by a second-order reaction between adrenochrome and acid. The product of this step cannot be isolated but is probably 1-methylindole-5,6-quinone and gives a derivative with 1,4-naphthaquinone; it polymerises rapidly by way of dimers and oligomers, with absorption spectra characteristic of indolylindolequinone groups. The growing polymer chain contains oxidisable groups which reduce part of the monomer quinone to 5,6-dihydroxy-1-methylindole. The monomer quinone also reacts with indole itself, giving a melanin-like copolymer.

STUDIES of melanin formation *in vitro* have mostly been concerned with oxidative processes, enzymic or otherwise, especially the oxidation of 5,6-dihydroxyindole (a probable intermediate *in vivo*) and analogous compounds. The conversion of these into melanins involves oxidation of the diol system and polymerisation, and the products are black polymeric pigments, apparently without regular structure, containing reversibly oxidisable and reducible groups and susceptible of further oxidation. The most questionable details are of two kinds: first, the site of reactions between the indole nuclei and, secondly, the nature of the reacting species. The first has received considerable attention without reaching finality; the second, in particular the extent to which oxidation proceeds, accompanies, or follows the polymerisation steps, is the subject of this paper. Consider the formation of a hypothetical linear phenolic polymer (I) from 5,6-dihydroxyindole; such a polymer, corresponding to minimal oxidation, is isomeric with indole-5,6-quinone (II), and in terms of the model reaction, indole + quinone ⟶ indolylquinol,[1] could be formed from the quinone (II) by self-combination. However, it could equally well arise by initial attack of the quinone or the corresponding semiquinone free-radical on the parent dihydroxyindole, with most of the oxidation occurring between or after polymerisation steps.

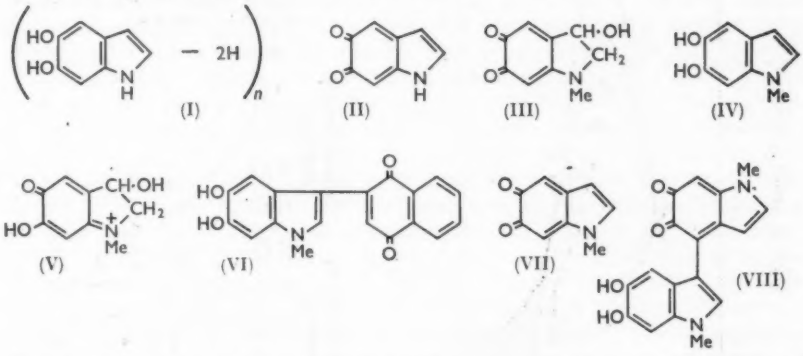
For the study of such a situation a non-oxidative process of melanin formation offers advantages; such a process occurs when solutions of adrenochrome (III) are stored, especially at acid pH, even in the absence of air. Observations on this instability of adrenochrome have been summarised by Heacock.[2] Visually the reaction has three phases. First, addition of acid to adrenochrome causes partial or complete discharge of the red colour, restored only by immediate neutralisation; secondly, various rather dirty

[1] Bu'Lock and Harley-Mason, *J.*, 1951, 703.
[2] Heacock, *Chem. Rev.*, 1959, **59**, 181.

purple shades appear; thirdly, a black precipitate or suspension is formed. With only traces of acid the phases are merged. Bouvet [3] noted that below pH 2 adrenochrome was reversibly transformed into a labile yellow material; Harley-Mason [4] observed that an unbuffered solution of fairly pure adrenochrome, stored in absence of air, afforded *ca.* 75% of black pigment, with 5,6-dihydroxy-1-methylindole (IV) as the main by-product. Melanins formed in this way are similar to those formed oxidatively, differing mainly in a somewhat greater solubility in pyridine or aqueous alkali, which suggests a lower molecular weight or a higher proportion of phenolic groups. The presence of the *N*-methyl group is unlikely to have a significant effect since oxidation of compound (IV) yields a normal melanin.[4]

In the present work the decomposition of adrenochrome in acid solutions, at a range of concentrations and acidities, was followed quantitatively with a recording spectrophotometer. After preliminary experiments in which air was excluded without affecting the reaction, no special precautions were taken, and in general the experiments were very reproducible. The effect of various added substances on the overall process was also studied.

On addition of acid to adrenochrome (III) ($\lambda_{max.}$ 300, 485 mμ) there is formed, in less than one second and reversibly, a yellow salt (conjugate acid), probably (V), since its absorption spectrum, seen briefly in strongly acid solutions or deduced from difference spectra (Fig. 1), shows $\lambda_{max.}$ *ca.* 400 mμ and somewhat resembles that of simple *para*-quinones. For the transformation of the quinone (III) into product (V) there are isosbestic points at 315 and 410 mμ, and from measurements over a range of adrenochrome and acid concentrations the titration curves of Fig. 2 can be calculated, from which the pK of adrenochrome is *ca.* 1·2. If the mixture of compounds (III) and (V) is immediately neutralised with alkali, most of the adrenochrome is regenerated but otherwise the solution shows marked instability. When free adrenochrome predominates in the mixture (*i.e.*, at pH > pK) the decomposition can be followed by the falling absorption at 485 mμ, as



shown in Fig. 3, and in such sets of curves a regular sequence of events is observed. First, the maximum at 485 mμ steadily diminishes and there are isosbestic points at 410 and *ca.* 540 mμ, but then the maximum, whilst still falling in intensity, begins to move to longer wavelengths, up to but not more than 540 mμ, and successive curves no longer intersect at 540 mμ. Next the maximum at 540 mμ falls away without changing its position. Finally there is a much slower (and possibly not anærobic) phase in which the absorption throughout the visible region may increase slightly. The phase with $\lambda_{max.}$ *ca.* 540 mμ is the " purple " phase observed visually, and in slow reactions (small amounts of acid) it is less well marked as a distinct phase; the following phase is that in which

[3] Bouvet, *Ann. Pharm.*, 1949, **7**, 514.
[4] Harley-Mason, *J.*, 1950, 1276.

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black pigment is formed. The observations are summarised in Fig. 4, which shows the change in optical density at 485 and 540 mμ in solutions of various acid concentrations.

Allowance being made for the equilibrium between compound (III) and (V), the results of series of observations like those of Fig. 3 were used to derive the rates of disappearance of adrenochrome from solutions of varying composition, and these rates

FIG. 1. *Absorption spectra*: (1) *adrenochrome*, (2) *conjugate acid of adrenochrome*, (3) *melanin from adrenochrome*. (*All solutions*: 0·05 *mg. per ml. in* 1 *cm. cell.*)

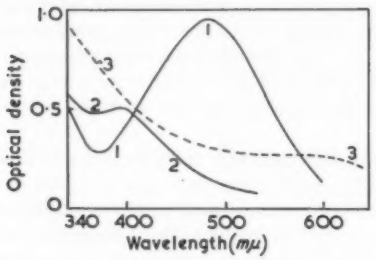


FIG. 2. *Equilibrium between adrenochrome base and conjugate acid.*

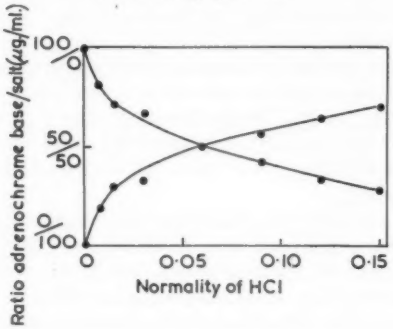


FIG. 3. *Successive absorption spectra* (*2-minute intervals*) *of adrenochrome* (1·0 *mg. per ml.*) *in* 0·03N-HCl. (*Absorption max.* ▲.)

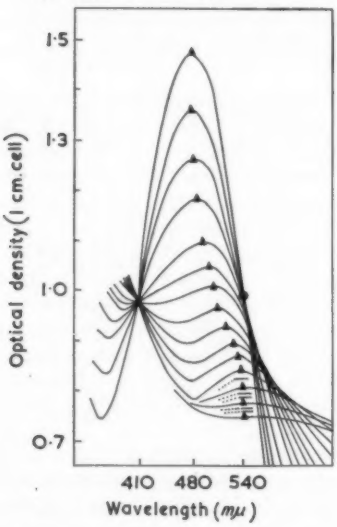
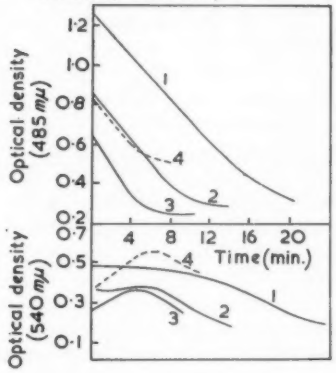


FIG. 4. *Variations of optical density at* 485 mμ (*upper curves*) *and* 540 mμ (*lower curves*): (1) *acid* 0·03N, (2) *acid* 0·07N, (3) *acid* 0·09N, (4) *as* (2) *plus* 1·0 *mg. of indole per ml.* (*Adrenochrome* 0·1 *mg. per ml. in all cases*; 1 *cm. cell.*)



were found to be directly proportional to the concentration of the salt (V) (with $k = 1{\cdot}0$ min.$^{-1}$), or, what is equivalent, to the product of the concentrations of adrenochrome base (III) and mineral acid. This relation holds over the range of adrenochrome concentrations of 0·05 to 0·5 mg. per ml. and with acid solutions of up to nearly 0·1N. In more acid solutions containing initially a preponderance of compound (V), the process is so rapid that its study is more difficult: declining absorption at 400 mμ appears to be accompanied by an increase below 400 mμ and followed by development of a maximum at *ca.* 540 mμ

(shifted towards 600 mμ in solutions more than 1N in acid) which subsequently declines into general absorption.

The overall reaction in the decomposition of adrenochrome in the absence of air is thus limited in rate by an acid-catalysed reaction of the first order in adrenochrome. It is also apparent (cf. especially Fig. 4) that the product of this reaction is not the material with absorption at 540 mμ, but a precursor of that material, itself not detected spectroscopically. Some indications of its nature are available. For instance, if acidification of the quinone (III) is carried out in the presence of 1,4-naphthaquinone no melanin is formed, but from the blue-green product the indolylnaphthaquinone derivative (VI) can be isolated. This is known to be formed from the dihydroxyindole (IV) and 1,4-naphthaquinone,[1] but the quinol (IV) is only formed from the quinone (III) in reductive processes, so that in the present circumstances the formation of product (VI) is best ascribed to a reaction of 1-methylindole-5,6-quinone (VII). The reactions of acidified adrenochrome with indole and cysteine and the formation of quinol (IV) as a by-product of polymerisation, as discussed later, also point to the formation of a quinone (VII) from adrenochrome on acidification. This is also probable on more general grounds: (VII) is the likely product of an acid-catalysed reaction (dehydration), and the 3-hydroxy-group of adrenochrome must be removed at an early stage in the melanin-forming process, since the later stages are closely analogous to those in oxidative melanin formation from 5,6-dihydroxyindole, in which a 3-hydroxy-group is not involved.[4] The formation of quinone (VII) being rate-limiting, and its disappearance as well as its formation being acid-catalysed, no accumulation of it need be expected under the experimental conditions. Other workers have attributed to quinones such as (VII) absorption maxima at *ca.* 360 mμ [5] or at *ca.* 470 mμ,[6] a disagreement which the present evidence does nothing to resolve.

To indole-5,6-quinones such as (VII) has also been attributed [7] the absorption at *ca.* 540 mμ in the " purple " phase of melanin formation, but, as shown by the present work, this material is not the *initial* product of the decomposition of adrenochrome. On the other hand, it is closely related spectroscopically to the final polymeric product. Robertson and his co-workers [5] have particularly considered this phase in oxidative melanin formation and pointed out the resemblance between the absorption spectra obtained and those of indolylbenzoquinones.[1] The comparison is apt, and on general grounds such a chromophore can only be accommodated in a dimer, *viz.*, a dihydroxyindolylindolequinone or a related oligomer. One possible structure for such a dimer is (VIII); its formation from the quinone (VII) would be analogous to the postulated reaction between (VII) and 1,4-naphthaquinone, giving (VI), and to the general reaction [1] between quinones and indoles.

However, the " purple " stage is not attributed uniquely to the formation of an intermediate dimer, and indeed its *gradual* transformation into black polymer indicates a more complex situation. Some insight into the process, as viewed spectroscopically, can be had from *a priori* considerations. If an oxidative transformation of benzene through biphenyl into polyphenyls could be observed spectroscopically, the spectra [8] would show a continuing shift to longer wavelengths for the *para*-polyphenyls, where conjugation is extended without limits, but no comparable shift for the *ortho*- or *meta*-series where increasing conjugation is subject to steric and electronic restrictions. An analogous actual case [9] is the oxidation of 1,8-dihydroxynaphthalene to a 4,5-linked polymer, in which a shift to longer wavelengths occurs when the dimer (a tetrahydroxybinaphthyl) is formed, but is not continued during the further transformation into a sterically hindered polymer. The effective chromophore of this polymer is therefore that of successive dimer units in the chain, but since these are not all quite identical, their combined spectrum

[5] Beer, Broadhurst, and Robertson, *J.*, 1954, 1947.
[6] Cromartie and Harley-Mason, *Biochem. J.*, 1957, **66**, 713.
[7] Mason, *J. Biol. Chem.*, 1948, **172**, 83.
[8] Gillam and Hey, *J.*, 1939, 1170.
[9] Allport and Bu'Lock, *J.*, 1960, 654.

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shows a marked broadening of the " fundamental " peaks. The case of a melanin-like polymer is more complex though still analogous; there are present both oxidised (quinonoid and reduced aromatic units, but for long-wavelength absorption the relevant groups are the quinonoid units and their attached neighbours. From considerations of oxidation–reduction equilibria (see below) the attached units will mainly be in reduced forms, and on general (steric) grounds and from data on the spectra [1] of di-indolylquinones and di-quinonylindoles not more than one of them will be greatly effective in extending the quinone chromophore. Though the exact absorption characteristics of each such chromophore will reflect the structure and stereochemistry of a part of the polymer assembly, the basic structure will be that of corresponding dimers. Thus, while transformation of monomer, *e.g.*, (VII), into dimer, *e.g.*, (VIII), modifies the chromophore radically, further transformations into polymer will appear spectroscopically as the gradual imposition of a somewhat random series of distortions until the specific absorption curve is replaced by one of general but analogous absorption. This is precisely what is observed in the final stages of both the oxidative melanisation of 5,6-dihydroxyindole at neutral pH [7] and the acid-catalysed melanisation of adrenochrome as in Fig. 3; the maximum at *ca.* 540 mμ falls whilst the curve as a whole becomes flatter, but there persists a more or less well-defined inflexion at corresponding wavelengths (cf. Fig. 1). The intermediate species with $\lambda_{max.}$ *ca.* 540 mμ are therefore identified as dimers, oligomers, and ultimately " residual chromophores," with 5′,6′-dihydroxyindolylindole-5,6-quinone structures such as (VIII).

The polymerisation process in the acid-catalysed melanisation is therefore envisaged as beginning with self-combinations of the quinone (VII) to give the dimer (VIII) or isomers, such a reaction [1] apparently being acid-catalysed, followed by reaction between dihydroxyindolyl groups in the dimer or oligomers with free or combined indolequinone groups. Since the reacting groups are not necessarily monofunctional a branched or cross-linked polymer will result.[1] If under anærobic conditions this were the only process the final polymer would contain only one quinonoid group per molecule, which is certainly not the case. However, the oxidation potential of an indolequinone such as (VII) should be lowered by a dihydroxyindolyl substituent, as in (VIII); consequently, dihydroxyindolyl residues in the reduced polymer will be oxidisable by the free quinone (VII), giving quinonoid groups in the polymer and explaining the observed formation [4] of the dihydroxyindole (IV). The extent of such processes will be limited, since the effect of substituting a *quinonoid* group for hydrogen in (VII) would be to *raise* the oxidation potential; consequently, in a linear or random polymer not more than half the units will be readily oxidised by the free quinone. An observed polymer yield of *ca.* 75%, implying about one-third complete oxidation in the polymer, thus seems not unreasonable.

The preceding arguments imply the ready reactivity of quinones such as (VII) both towards indoles with cationoid reactivity and with quinones susceptible to nucleophilic addition. The formation of the naphthaquinone derivative (VI) is evidence for the latter reaction; evidence for the reactivity of (VII) towards indoles was also obtained. As shown in Fig. 4, the addition of indole (or of 5,6-diacetoxyindole) to acidified adrenochrome solutions has no effect on the rate of disappearance of adrenochrome, but markedly accelerates the appearance of " dimer-type " absorption around 540 mμ. Eventually a polymer is precipitated, which is soluble in methanol and thus of rather low molecular weight, and smoke-grey in colour, implying a high proportion of non-quinonoid units. In methanol solution the polymer shows absorption around 300 mμ many times more intense (compared with the visible absorption) than any normal melanin, which is ascribed to the incorporated indole units; on the other hand, the intensity of the visible absorption (compared with that of the original adrenochrome) is greater than in the absence of added indole (cf. Fig. 4), *i.e.*, by supplying a substitute for the reduced groups of the melanin the added indole increases the yield of oxidised chromophoric units from the adrenochrome. Adrenochrome itself does not react at neutral pH with indole or with 1,4-naphthaquinone, and in the acidified system no reaction with a 10-fold excess of tyrosine, phenylalanine,

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p-aminobenzoic acid, or tryptophan was detected, though a reaction of indolequinones with free amino-groups might be expected at higher pH. With cysteine a reaction analogous to that observed with enzymically oxidised hydroxyindole [10] apparently competes, in the acidified system, with reduction of the adrenochrome.

The foregoing observations are clearly also relevant to the oxidative route to melanins, in which indolequinones are differently generated. Work now in progress confirms this. The copolymerisation with indoles may also have a bearing on the structure of natural and enzymically produced melanins. Nicolaus *et al.*[11] have recently obtained evidence for the presence of up to 20% of units derived from 5,6-dihydroxyindole-2-carboxylic acid in sepia melanin; this acid could be an alternative product to 5,6-dihydroxyindole in the oxidation of tyrosine and 3,4-dihydroxyphenylalanine, and though not itself oxidisable to a melanin, its incorporation into an indolequinone-derived polymer by a copolymerisation analogous to that established for indole at acid pH now appears very plausible. In the enzymic process a similar direct incorporation of other potentially anionoid substances such as tyrosine or 3,4-dihydroxyphenylalanine might also be expected under conditions where these were present during the generation of the indole-5,6-quinone.

Experimental

Crystalline adrenochrome was prepared by the Sobotka and Austin's method [12] and stored at −25° until required; standard solutions of 1·0 mg. per ml. were then made up in deionised water. From measured volumes of this and of standardised hydrochloric acid, reaction mixtures, with adrenochrome from 0·05 to 1·0 mg. per ml. and acid from 0·007 to 1·5N, were made up directly in 1 cm. optical cells (capacity 4·0 ml.) placed in the beam of a Carey recording spectrophotometer. Spectra were recorded from 650 to 350 mμ at measured intervals of 1·5 to 2·0 min. (cf. Fig. 3). At the scanning speeds used there was an uncertainty of *ca.* 5 mμ in the wavelength scale, and the reported maxima are not necessarily comparable with those measured in static systems.

With an adrenochrome concentration of 0·1 mg./ml. and concentrations of acid C_H from 7×10^{-3} to $1{\cdot}5 \times 10^{-1}$N the values of the optical density at 490 mμ, D_{490}, were measured immediately on mixing. By extrapolation of a plot of D_{490} against $1/C_H$ a value for D_{490} for complete salt formation was obtained and, by using this and the presumption that base and salt absorb independently, values of C_A and C_{HA}, concentrations of adrenochrome base and salt, corresponding to the D_{490} values were computed. The variation of C_A with C_H approximates to the theoretical, and values of C_A and C_{HA} are plotted against C_H in Fig. 2. The spectrum shown for the salt in Fig. 1 was computed from that of a mixture ($C_H = 6 \times 10^{-2}$N) for which C_A and C_{HA} had been thus established. For a rate plot, observed rates of decrease of D_{490} with time were multiplied by the ratio of D_{490} before and immediately after acidification, to correct for the proportions of the total adrenochrome present as two differently-absorbing species.

For copolymerisation with indole, the solution contained 0·1 mg. of adrenochrome per ml., 1·0 mg. of indole per ml., and 0·07N-hydrochloric acid; on completion of the reaction the precipitate was allowed to settle, taken up in aqueous alkali, precipitated with hydrochloric acid, centrifuged down, and dissolved in methanol for measurement of the absorption spectrum. For the preparation of the quinone (VI), 1 drop of concentrated hydrochloric acid was added to 10 ml. of an aqueous-ethanolic solution containing 10 mg. of adrenochrome per ml. and 5 mg. of 1,4-naphthaquinone per ml. The greenish-blue mixture was extracted with chloroform, the extract evaporated, and the residue purified by chromatography on neutral alumina in chloroform–benzene to give 2-(5,6-dihydroxy-1-methyl-3-indolyl)-1,4-naphthaquinone as violet crystals, giving a blue-green colour with alkali and identified with authentic material [1] by absorption spectra and paper chromatography in aqueous butanol.

[10] H. S. Mason and E. W. Peterson, personal communication.
[11] Nicolaus, Piatelli, and Narni, *Tetrahedron Letters*, 1959, No. 21, 14.
[12] Sobotka and Austin, *J. Amer. Chem. Soc.*, 1951, **73**, 3077.

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12. *Studies in Adsorption. Part XII.*[1] *Mechanism of Adsorption of Aromatic Hydrocarbons by Chromatographic Alumina.*

By C. H. Giles and R. B. McKay.

Naphthalene is adsorbed by chromatographic alumina from 2,2,4-trimethylpentane; 2,3-benzanthracene, phenanthrene, and pyrene, but not naphthalene, are adsorbed from xylene. Only a minute fraction of the available surface (*ca.* 0·1%) is covered. S-Shaped isotherms are obtained. It is suggested that a π-electron complex is formed between the hydrocarbon and a few sites, probably aluminium atoms, exposed by mechanical damage, on the outer surface of the oxide. The nature of the adsorption isotherms suggests that the hydrocarbon molecules are adsorbed in small clusters, in which they are stacked face-to-face edge-on to the oxide surface.

A previous paper[2] described an investigation of the mechanism of adsorption of ionic and polar non-ionic solutes by chromatographic alumina. It was shown that the former are adsorbed mainly by an ion-exchange process and perhaps by covalent-bond salt formation, and the latter by hydrogen bonding (OH···O; NH···O; and CH···O bonds were detected). Chelating compounds form complexes with the substrate.

Non-polar solutes were not studied. Alumina columns are, however, used for the separation of unsaturated hydrocarbons, which generally separate according to the length of their conjugate system or the number or coplanarity of the aromatic nuclei, those containing the longest system or the most nuclei being the less readily eluted.[3-5] This appears to indicate that aromatic hydrocarbons are adsorbed on alumina, and therefore that some adsorption mechanism other than those detected for ionic and polar solutes is operating.

Basu[6] suggested that this mechanism is one of molecular complex formation, facilitated by (*a*) a high electron affinity of one component and (*b*) a low ionisation potential of the other, and pointed out that, on the assumption that the energy of the top-filled orbital of a conjugated organic molecule calculated by the LCAO method gives a rough estimate of (*b*), the separations in two series of compounds (five condensed-ring aromatic hydrocarbons and four αω-diphenylpolyenes) agree in both cases with this hypothesis. In the previous paper[2] it was suggested that the mechanism might be either (*a*) formation of a complex between the π-electrons of the hydrocarbon and the alumina (a similar mechanism to that suggested by Basu) or (*b*) a partition effect, in which the rate of downward movement of solute is determined by the rate of its transfer from the initial solvent holding it at the top of the column to the eluting solvent. The present investigation was made to examine these suggestions.

While the present research was in progress Klemm *et al.*[5a] reported an investigation of

[1] Part XI, Giles, MacEwan, Nakhwa, and Smith, *J.*, 1960, 3973.
[2] Cummings, Garven, Giles, Sneddon, and Stewart, *J.*, 1959, 535.
[3] Williams, "An Introduction to Chromatography," Blackie and Son Ltd., London, 1946.
[4] Strain, "Chromatographic Adsorption Analysis," Interscience Publishers Inc., New York, N.Y., 1942.
[5] (*a*) Klemm, Reed, Miller, and Ho, *J. Org. Chem.*, 1959, **24**, 1468; (*b*) see other references in (*a*).
[6] Basu, *Chem. and Ind.*, 1956, 764.

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the adsorption of aromatic hydrocarbons on alumina from binary mixtures of various hydrocarbons, and judged the degree of separation of more than 40 pairs by effluent analysis. The ease of absorption appeared to be governed by three qualitative rules, being favoured by increase in the number of double bonds present in the solute, increase in the degree of its co-planarity, and by a " symmetry rule."

In the present work isotherms (Fig. 1) were determined for several aromatic hydrocarbons from two solvents on Grade II and Grade I alumina.

Experimental

Substrate.—This was chromatographic alumina Type H (Savory and Moore) (Grade II),[2] specific surface area, by phenol adsorption,[2] 5×10^5 cm.^{2} g.$^{-1}$, used without further treatment, or after conversion into Grade I. This conversion was made by roasting the alumina in a muffle furnace at *ca.* 700° for 5 hr., with frequent stirring, and subsequent cooling *in vacuo*; the product was stored in a tightly sealed jar.

Effect of Dehydration of Substrate.—Roasting reduced the weight by 5·9%. Ignitions of alumina (corundum) up to *ca.* 400° result in very little loss of chemically bound water, the surface layer approximating to $Al(OH)_3$ being retained. At higher temperatures partial or complete dehydration, depending on the temperature, takes place to give a surface approximating to either AlO·OH or γ-Al_2O_3.[7] In the present material, if the 5·9% loss on roasting is taken to be that of a monolayer of water molecules each occupying 8·2 Å^2 (the approximate cross-section, edge-on), it represents *ca.* 16×10^5 cm.^{2} of extra surface per g. of powder, so that Grade I powder would on this assumption have 4·5 times the available active surface of Grade II. This figure agrees well with the 5·3-fold greater maximum adsorption of phenanthrene (Fig. 1, *a*—*c*) on Grade I than on Grade II powder. (An attempt was made to rehydrate Grade I to Grade II powder by storing it under moist air until it had increased 5·9% in weight, but there were experimental difficulties in stopping the increase at the correct value. The product had only *ca.* 60% of the phenanthrene-adsorbing capacity of the original Grade II powder; cf. Fig. 1*c*.)

Reagents.—The solutes were commercial products, purified by distillation or sublimation. The solvents were B.D.H. " Laboratory Reagent " grade 2,2,4-trimethylpentane (" Special for spectroscopy "), and xylene (mixed isomers) redistilled to b. p. range 138—142°. Even after distillation there appeared to be a trace of an impurity in the xylene which coloured Grade I alumina pale yellow. This was removed by shaking the solvent with charcoal and filtering. The impurity did not, however, appear to be adsorbed by Grade II alumina.

2,3-Benzanthracene is sparingly soluble, and solutions were prepared by leaving the solid in contact with the cold solvent for several days, and then filtering. All other solutions were freshly prepared just before use.

Adsorption and Analysis.—The hydrocarbons are adsorbed to a much smaller extent than the solutes previously used,[2] and the methods were accordingly modified to increase their sensitivity: 2 g. samples of alumina and 5 c.c. of test solution in ground-glass, stoppered tubes were shaken by hand for 10—15 min. at room temperature. (Preliminary rate tests showed that adsorption was complete in a few minutes.) The tubes were next set aside for 5 min. and a portion of each solution was then removed by decantation for spectrophotometric analysis, by the Unicam S.P. 500 instrument. Each result was obtained from the mean of 6—10 successive readings on each solution. This procedure occupied 30—60 min., and consequently, to ensure uniform treatment, each solution was treated separately with alumina immediately before analysis.

Phenanthrene was very little adsorbed, and to avoid possible inaccuracies caused by the necessary five-fold dilution of the test solutions for analysis at $\lambda_{max.}$, spectrophotometric readings on this solute were taken at a wavelength of *minimum* adsorption, at which the optical density is about one-fifth that at the maximum. All other solutes were determined at a wavelength of maximum absorption, if necessary after dilution with fresh solvent. 1 mm. or 10 mm. cells were used.

The isotherms for pyrene and 2,3-benzanthracene could not be taken as far as the plateau, because of the scarcity or the low solubility of the solutes.

[7] O'Connor, Johansen, and Buchanan, *Trans. Faraday Soc.*, 1956, **52**, 229.

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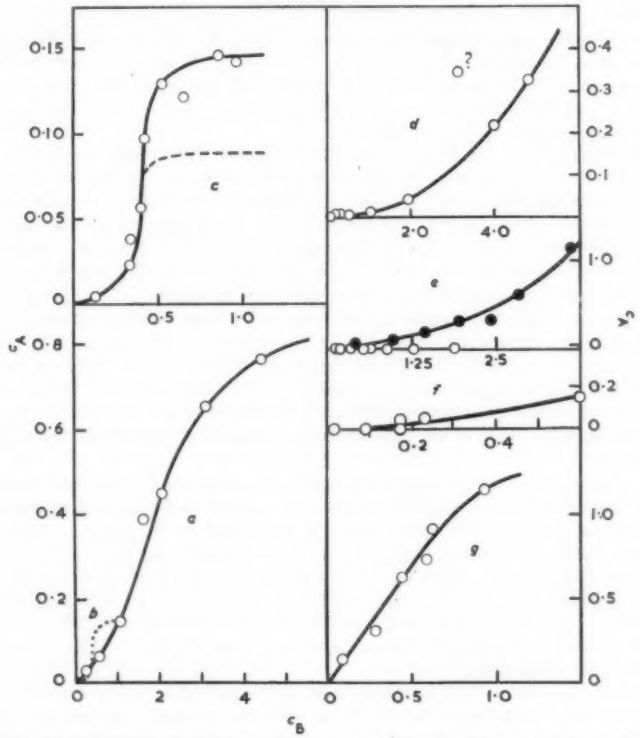
Tests with Cellulose, Graphite, and Silica.—Parallel tests with these substrates gave no evidence of adsorption of phenanthrene by cellulose (Whatman chromatographic powder) or silica (MSC powder [1]), from benzene or xylene. The tests with graphite were inconclusive because a significant increase in optical density (at 3240 Å) of the solutions occurred. The increase was independent of solute concentration, and may have been caused by preferential adsorption of solvent.

FIG. 1. *Adsorption isotherms of aromatic hydrocarbons, etc., in xylene (except where indicated otherwise) on chromatographic alumina at 20°.*



c_A is the equilibrium concentration on the alumina (mmole/kg.) and c_B that in the bath (mmole/l.).
(*a*) *Phenanthrene (Grade* I *alumina).* (*b*, *c* *) *Phenanthrene (Grade* II *alumina); broken line shows isotherm from recycled Grade* II *(see Experimental section).* (*d*) *Pyrene (Grade* II*).* (*e*) *Naphthalene (Grade* II*) from 2,2,4-trimethylpentane; open circles show result of test with xylene solvent.* (*f*) **2,3-***Benzanthracene (Grade* II*).* (*g*) *Oxidation product of phenanthrene (Grade* II*).*

* Curve *c* is repeated as *b* for comparison with *a*.

Adsorption of Phenanthrene Oxidation Product.—The optical density of phenanthrene solutions increased considerably on exposure to light for several days. The product was more readily adsorbed than unchanged phenanthrene and appeared to give an *L* isotherm, indicative of a polyfunctional solute oriented flat at the surface; [1] it may be biphenic acid (Fig. 1*g*).

Results and Discussion

Mechanism of Adsorption.—Positive adsorption was detected with all the solutes except benzene in 2,2,4-trimethylpentane and naphthalene in xylene, and the rapidity of adsorption shows that it occurs only on the external surface of the particles. This agrees

with the evidence of Klemm *et al.*[5a] that steady-state processes are occurring in the column, deduced from the applicability of the " law of inequalities," *i.e.*, if, amongst three hydrocarbons, A, B, and C, A > B and B > C in ease of adsorption, then also A > C.

Naphthalene is readily adsorbed from an aliphatic solvent, which presumably is itself unadsorbed. The non-adsorption of naphthalene from xylene must be the result of preferential adsorption of the aromatic solvent molecules at the very limited number of sites.

The amount of phenanthrene adsorbed is substantially higher on Grade I than on Grade II material, but the apparent affinity of phenanthrene is actually lower on Grade I than on Grade II (−3·7 and −5·1 kcal./mole respectively *).

The roasting treatment used to prepare Grade I material removes firmly bound water. Therefore, though Grade I oxide has higher affinity for water than Grade II, it has lower affinity for an aromatic hydrocarbon, but more available sites. This suggests that water and hydrocarbons are adsorbed at different sites. Water is probably hydrogen-bonded to oxygen, and it may screen some of the sites suitable for hydrocarbons. The absence of any adsorption by silica or cellulose (see p. 60) appears to show that neither oxygen atoms nor hydroxy-groups are sites for the hydrocarbons. Therefore the sites are probably aluminium atoms. The substrate is the γ-form of alumina, in which each aluminium atom is surrounded by six oxygen atoms, and is thus normally inaccessible to molecules adsorbed at the surface. The structure may, however, be distorted by abrasion in grinding. O'Connor *et al.*[7] point out that, at a freshly fractured surface, co-ordination of some ions must be incomplete. They found that freshly ground corundum always had a positive zeta-potential in water, indicating the surface ionisation of hydroxyl groups, following extensive hydration of aluminium ions to give a layer of $Al(OH)_3$. The hydrocarbons probably form a π-electron complex with the small proportion of aluminium atoms that happen to be exposed at the surface. Calculation from the position of the plateau in the phenanthrene isotherm shows in fact that only a very small fraction (*ca.* 0·06%) of the alumina surface is covered at saturation. Pyrene and 2,3-benzanthracene would clearly (see Fig. 1) cover rather more than this proportion, but still only a fraction of the total surface.

Klemm *et al.*[5a] reached a similar conclusion, *viz.*, that the adsorption takes place on " active spots " of the alumina surface in a π-type (outer- or charge-transfer) complex; in addition they consider that the adsorption is unimolecular; also that it is flatwise, but the present results do not support the latter suggestion (see p. 62).

The following data, quoted by Basu,[6] agree with the hypothesis, so also does the improved adsorption produced by (*a*) substitution of methyl or ethyl groups into aromatic hydrocarbon nuclei,[5a] and (*b*) an increase in the number of methyl groups substituted in the benzene nucleus,[5a] since these groups increase the electron availability in the nucleus.

Compound	Energy of topmost filled orbital	Position on Al_2O_3 column
Pentacene	0·205	Top
Tetracene	0·276	↓
Anthracene	0·379	↓
Naphthalene	0·535	↓
Benzene	0·800	Bottom
2,3-Benzanthracene	0·276	Top
1,2:6,7-Dibenzanthracene	0·500	Bottom

Water molecules must be attached very firmly to the oxygen atoms. This may increase the electropositivity of the neighbouring aluminium atoms, and so be responsible for the lower affinity of the surface for phenanthrene when water is removed to form

* Calculated from the expression, $-\Delta\mu^\circ = -RT \ln c$, where c is the solute concentration in a solution at equilibrium with alumina that has adsorbed half the maximum amount of solute. The value for pyrene on Grade II alumina is numerically less than −3·3 kcal./mole.

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Grade I material. The donor molecule requires a low ionisation potential, and this is favoured by an increase in the length of its conjugate system.

The alumina–hydrocarbon bond here suggested may have some similarity to the complexes between benzene and silver cations [8] and between the π-electrons of graphite and alkali-metal cations.[9]

Orientation of Adsorbed Hydrocarbon Molecules.—A recent investigation [1] into the relation between solution adsorption mechanisms and the shape of the resulting isotherms has shown that: (i) whenever the *S*-isotherm (*i.e.*, convex to solution-concentration axis)

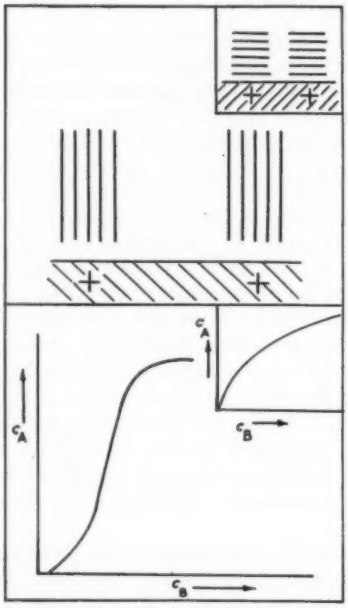

FIG. 2. *Adsorption mechanism of aromatic hydrocarbons on alumina.*

Top: *Showing suggested stacking of isolated clusters of planar aromatic molecules (end-on) at* Al^+ *atoms exposed at the surface.*

Bottom: *Adsorption isotherm obtained, characteristic of end-on adsorption*

Insets: *Alternative stacking (not favoured) and corresponding isotherm.*

is obtained, the most likely orientation of the adsorbed solute molecules is end-on to the surface, and in side-by-side association; (ii) when flatwise orientation occurs the normal isotherm (class "*L*," concave to solution-concentration axis) is always obtained; (iii) when further adsorbed layers very readily build up on the first, the curve rises steadily beyond the first inflection. All the present isotherms are of *S*-type; thus apparently the hydrocarbon molecules are adsorbed end-on, and not, as might at first sight appear most likely, flatwise. The surface coverage is extremely low, as already discussed, so the molecules appear to be stacked in small clusters at very isolated sites (Fig. 2). The reduction in adsorbability that follows substitution with alkyl groups larger than ethyl [5a] is, on this hypothesis, the result of the steric hindrance of face-to-face packing.

Aromatic nuclei most readily associate face-to-face. Therefore flatwise adsorption would lead to the ready build-up of further layers on top of the first, and the isotherm would have a normal (concave) lower part, with an inflection followed by a steadily rising upper portion (*i.e.*, *L3a* type,[1] cf. Fig. 2, bottom, inset). (This type of curve has been observed for flatwise adsorption of layers of a merocyanine dye on silver halide, see Fig. 6*a*, ref. 1.)

[8] Mulliken, *J. Amer. Chem. Soc.*, 1952, **74**, 811; *J. Phys. Chem.*, 1952, **56**, 801; Smith and Randle, *J. Amer. Chem. Soc.*, 1958, **80**, 5075.
[9] Croft, *Quart. Rev.*, 1960, **14** 1.

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Part XI, Errata.—In Table 1; *S* curves, entry for phenol, *S*1 isotherm, *for* ref. 2*a read* ref. 12*a*; *L* curves, entry for phenylazo-2-naphthol, *L*2 isotherm, *for* ref. 12*a read* ref. 14; *C* curves, entry for azobenzene, *for* isotherm *C*1 *read* *C*1(?); footnote ¶ *should read* ref. 12*b*.

p. 3390, line 13, *for* refs. 7,5 *read* ref. 15.

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13. *Kinetics of the Bromination of Some Anisoles and Phenols.*

By R. P. Bell and D. J. Rawlinson.

Kinetic measurements have been made on the bromination of four anisoles and six phenols in aqueous solution. The potential of a redox electrode was used to follow the disappearance of bromine in very dilute solution, and velocity constants up to 3×10^4 l. mole^{-1} sec.$^{-1}$ were measured. Measurements at varying acidities were used to derive separately the bromination velocities of phenol molecules and phenoxide ions, the latter having velocity constants up to 8×10^9 l. mole^{-1} sec.$^{-1}$. In most of the reactions studied no reaction of tribromide ions could be detected, but in the bromination of phenoxide ions their reactivity amounted to 1—3% of that of molecular bromine.

Previous work with aromatic amines [1] and with *m*-nitrophenol [2] has shown that it is possible by means of electrical methods to measure the very high rate constants (10^2 to 10^{10} l. mole^{-1} sec.$^{-1}$) for reaction of these substances with bromine. With the more reactive species, such as the dimethylanilines and the *m*-nitrophenoxide ion, it is possible to detect reaction with the tribromide ion as well as with molecular bromine, but with the less reactive *m*-nitrophenol molecule no reaction with tribromide ion can be detected. The present paper describes further work on *m*-nitrophenol by a different method, and measurements are also reported for other phenols and for anisoles, special attention being paid to the relative reactivity of Br_2 and Br_3^-.

Experimental

Materials.—Anisole and *o*-bromoanisole were fractionally distilled several times at atmospheric pressure, this process being repeated until the products from two successive fractionations gave identical kinetic results. No phenolic impurities were detectable by alcoholic ferric chloride. *p*-Bromo-, *m*-fluoro-, *o*-chloro-, and *p*-chloro-anisole were tested for phenolic impurities and distilled twice.

m-Nitrophenol, recrystallized three times from chloroform, had m. p. 98°. 2-Bromo-5-nitrophenol was prepared from *m*-nitrophenol as described by Henley and Turner [3] and recrystallized three times from carbon tetrachloride (m. p. 119°). 2,4-Dinitrophenol was recrystallized three times from water (m. p. 113°), and 2,6-dinitrophenol three times from aqueous alcohol (m. p. 61°). 2,4-Dibromophenol was prepared by brominating phenol as described by Pope and Wood: [4] the crude product was fractionally distilled at atmospheric pressure and then recrystallized from carbon tetrachloride (m. p. 35°). *p*-Bromophenol was recrystallized from carbon tetrachloride. Phenol was used without further purification.

[1] Bell and Ramsden, *J.*, 1958, 161.
[2] Bell and Spencer, *J.*, 1959, 1156.
[3] Henley and Turner, *J.*, 1930, 937.
[4] Pope and Wood, *J.*, 1912, **101**, 1824.

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All inorganic substances were of "AnalaR" quality, and the water used was redistilled from potassium permanganate in a glass still.

Measurement of Reaction Velocity.—The course of the reaction was followed by measuring the change of redox potential, as previously described.[1] A platinum-gauze electrode was used, in conjunction with a calomel electrode ending in a fine capillary tip. The potential was measured with a Tinsley potentiometer with mirror-galvanometer. The bromine concentration was usually followed over the range 10^{-5} to 10^{-3}M. Below about 10^{-5}M-bromine the potential does not decrease as quickly as it should do, and behaves erratically, often changing if the potentiometer is temporarily unbalanced. Erratic behaviour was sometimes encountered at higher bromine concentrations and could only be cured by remaking the electrode. It occurred less often if the electrode was kept immersed in a concentrated bromine solution between experiments. If the initial concentration of bromine is 10^{-6}M or less, an appreciable proportion of it reacts slowly with some impurity in the water used. This complication could be avoided by first adding enough bromine to react with the impurity and then leaving the solution until all the excess of bromine had evaporated: an experiment was then carried out in the usual way.

Provided that the concentration of bromide ion remains constant, the observed e.m.f. is given by

$$E = E_0 + 0{\cdot}0295 \log [Br_2] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

at 25°, the numerical factor at 0° being 0·0319. E_0 involves the bromide-ion concentration and any junction potentials present. If the organic substance is present in large excess the reaction will follow a first-order course, and the second-order velocity constant k at 25° is given by

$$k = -\frac{1}{c}\frac{\mathrm{d} \ln [Br_2]}{\mathrm{d}t} = -\frac{1}{c}\frac{\mathrm{d} \ln [Br_3^-]}{\mathrm{d}t} = \frac{-78{\cdot}2 \,.\, \mathrm{d}E}{c \,.\, \mathrm{d}t} \quad . \quad . \quad . \quad . \quad (2)$$

where c is the concentration of organic substance. At 0° the numerical factor has the value 71·7. Experiments carried out under these conditions did in fact give an accurately linear relation between E and t. If the organic substance is initially present in only moderate excess (say three-fold), c will become effectively constant after the bromine concentration has fallen by a power of ten (corresponding to 0·03 v), and a linear relation will hold after a curved initial section. Equation (2) can again be used, though the value of c will now differ from the initial concentration. If the concentrations of bromine and organic substance are more closely equivalent, then $[Br_2]$ can be calculated from equation (1), using the initial e.m.f. to obtain E_0, and the value of k calculated from the usual second-order equation, which can also be applied to the curved initial section in the previous case. All these methods have been used to calculate k, with concordant results. The values thus obtained do not discriminate between different forms of bromine (*e.g.*, Br_2 and Br_3^-) or of the organic substance (*e.g.*, phenol and phenoxide ion), so that they may vary with the concentration of bromide or hydrogen ions.

The volume of the reaction mixture was usually 100 ml., and it was stirred at a constant speed of 1500 r.p.m.; preliminary experiments showed that the same results were obtained with any speed between 800 and 2500 r.p.m. The reaction was started by adding one of the reactants from a calibrated pipette of about 1 ml. capacity. If possible, the organic substance was added last, so that the initial potential in the bromine solution could be measured. For the faster reactions it was convenient to set the potentiometer at successive 10 mv intervals, and to record the times at which the galvanometer spot passed through zero. By using initial concentrations down to 10^{-5}M it was possible to measure second-order velocity constants up to about 3×10^4 l. mole^{-1} sec.$^{-1}$.

Results for the Bromination of Anisoles.—Provided that Br_2 and Br_3^- are the only brominating species, the observed velocity constant for the bromination of an anisole should be represented by

$$k = (k_1 + Kk'_1[Br^-])/(1 + K[Br^-]) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where k_1 and k_1' are the second-order velocity constants for the reaction of anisole with the species Br_2 and Br_3^- respectively, and K is the equilibrium constant $[Br_3^-]/[Br_2][Br^-]$. K was assumed to be 16 at 25°, and 20 at 0°; these values are not accurately known,[5] but the conclusions reached are not affected by any reasonable choice of constants. The initial bromination

[5] Griffith, McKeown, and Winn, *Trans. Faraday Soc.*, 1932, **28**, 101.

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products are much less reactive towards bromine than the original substances, so that no correction is necessary for further bromination. Product analysis was not attempted, but there is good evidence [6,7] that bromination takes place mainly in the *para*-position.

The results are given in Tables 1 and 2. The velocity constants are expressed in l. mole^{-1} sec.$^{-1}$ and most of the values represent the mean of 2—6 experiments. Unless otherwise stated, the hydrogen-ion concentration was $9{\cdot}94 \times 10^{-4}$ (perchloric acid).

TABLE 1. *Bromination of anisole at* 0°.

(*a*) Variable [Br^-] and ionic strength (I); no added salt.

[Br^-]	0·199	0·494	0·586	1·48
k	1160	606	416	342
$k(1 + K[Br^-])$	5810	6610	8620	10,700

(*b*) Variation of [Br^-] at constant $I = 0{\cdot}5$ ($NaClO_4$ added).

[Br^-]	0·124	0·247	0·370	0·493
k	2140	1150	780	607
$k(1 + K[Br^-])$	7340	6860	6560	6620

(*c*) Variation of [Br^-] at constant $I = 0{\cdot}2$ ($NaNO_3$ added).

[Br^-]	0·00115	0·0107	0·0254	0·0500	0·149	0·178
k	5150	4500	3750	2790	1520	1200
$k(1 + K[Br^-])$	5270	5460	5620	5590	6040	5990

TABLE 2. *Bromination of* o-*bromoanisole at* 25°.

(*a*) Variation of [H^+] at constant $I = 1{\cdot}51$ and constant [Br^-] = 0·509 ($NaClO_4$ added).

10^4[H^+]	9·92	99·2	99·2	4980	9920
k	42·7	44·7	41·3	37·7	32·8

(*b*) Variation of [H^+] at constant I = 0·202 and constant [Br^-] = 0·0521 ($NaClO_4$ added).

10^4[H^+]	9·92	150	506
k	131	122	124

(*c*) Variable [Br^-] and I; no added salt.

[Br^-]	0·0134	0·0530	0·103	0·153	0·202
k	153	106	72	57	46
$k(1 + K[Br^-])$	185	194	189	196	194

(*d*) Variation of [Br^-] at constant $I = 0{\cdot}1$ ($NaNO_3$ added).

[Br^-]	0·00253	0·0225	0·0521	0·0719	0·100
k	216	158	110	92	72
$k(1 + K[Br^-])$	225	215	201	198	189

(*e*) Variation of [Br^-] at constant $I = 0{\cdot}2$ ($NaClO_4$ added).

[Br^-]	0·0521	0·102	0·151	0·200
k	131	84	61	46
$k(1 + K[Br^-])$	240	222	207	194

(*f*) Variation of [Br^-] at constant $I = 1{\cdot}51$ ($NaClO_4$ added).

[Br^-]	0·063	0·113	0·162	0·212	0·262	0·509	0·757	1·01	1·26	1·50
k	309	217	156	122	94·7	44·7	28·9	18·2	14·3	9·5
$k(1 + K[Br^-])$	621	610	560	536	492	409	379	313	288	238

(*g*) Variation of I at constant [Br^-] = 0·0521 ($NaClO_4$ or $NaNO_3$ added).

I	0·053	0·103	0·152	0·202	0·301	0·549	0·797	1·29	1·54
k($NaClO_4$)	106	110	119	131	135	178	229	318	370
k($NaNO_3$)	106	110	115	122	130	153	173	214	227

The results for *o*-bromoanisole are the more extensive, and will be considered first. Tables 2 (*a*) and (*b*) show that, as expected, the rate is little affected by hydrogen-ion concentration. The small decrease at high acidities is no greater than the salt effects discussed below. Equation 3 predicts that the quantity $k(1 + K[Br^-])$ should be independent of [Br^-] if molecular bromine is the only brominating agent, but should increase with [Br^-] if tribromide ion is also effective. Table 2 (*c*), in which only bromide is added, suggests no detectable effect of Br_3^-, while the experiments at constant ionic strength [2 (*d*), (*e*), and (*f*)] all show a decrease of $k(1 + K[Br^-])$ with [Br^-], which cannot be accounted for by equation 3. This behaviour is undoubtedly due to kinetic salt effects. Table 2 (*g*) shows that sodium perchlorate and sodium nitrate exert large positive effects of different magnitudes, and the results with varying bromide ion at constant ionic strength can be explained if potassium bromide exerts a smaller positive salt effect than either sodium perchlorate or sodium nitrate. A positive kinetic salt effect is to

[6] de la Mare and Vernon, *J.*, 1951, 1761.
[7] Stock and Brown, *J. Amer. Chem. Soc.*, 1960, **82**, 1942.

be expected on theoretical grounds[8] for a reaction between uncharged molecules in which charge separation occurs in the transition state, and there may also be a salt effect on the constant K. There is thus no experimental evidence for reaction between *o*-bromoanisole and tribromide ion, but by extrapolating the values in Table 2 (*c*) to infinite dilution we obtain a reliable value $k_1 = 185$ l. mole^{-1} sec.$^{-1}$ for the velocity constant of the reaction with bromine at 25° and zero ionic strength.

The results for anisole follow a similar pattern. The addition of high concentrations of bromide alone [Table 1 (*a*)] causes an increase in $k(1 + K[Br^-])$, which, taken by itself, would suggest $k_1'/k_1 \approx 0{\cdot}04$; *i.e.*, the reactivity of tribromide is about 4% of that of bromine. However, measurements with the ionic strength maintained at 0·2 by the addition of sodium nitrate show a considerably smaller increase [Table 1 (*c*)], and with addition of sodium perchlorate to an ionic strength of 0·5 [Table 1 (*b*)] a decrease is observed. There is thus no firm evidence for tribromide reactivity. The velocity constant for reaction with molecular bromine is about 6100 l. mole^{-1} sec.$^{-1}$ at 0°.

Some approximate measurements were made with a number of other anisoles at 25°, and the results are collected in Table 3, it being assumed that molecular bromine is the only active reagent. The value for *o*-nitroanisole is taken from the work of Wilson and Soper.[9]

TABLE 3. *Bromination of various anisoles at* 25°.

Subst.	—	*m*-F	*o*-Br	*o*-Cl	*p*-Br	*o*-NO_2
k_1	4×10^4	1×10^4	2×10^3	2×10^3	5	6×10^{-3}

Results for the Bromination of Phenols.—Solutions of phenols contain two reactive species, the molecule and the anion, and in principle both of these could react with either molecular bromine or the tribromide ion. Actually no evidence was found for reaction between phenol molecules and tribromide ion, and the results can be represented in terms of three velocity constants, k_1 (bromine + phenol), k_2 (bromine + phenoxide), and k_3 (tribromide + phenoxide). Provided that most of the phenol is present in the un-ionized form the expression for the observed velocity constant is:

$$k(1 + K[Br^-]) = k_1 + K_a(k_2 + k_3K\phi[Br^-])/f_\pm^2[H^+] \quad . \quad . \quad . \quad . \quad (4)$$

In this equation, K_a is the thermodynamic dissociation constant of the phenol, and $f_\pm^2$ the correction needed to obtain the phenoxide concentration in a solution of finite ionic strength: similarly, k_3 refers to zero ionic strength, and the factor $\phi = f_1^2/f_2$ represents the primary salt effect for the reaction between the two negatively charged ions. Most of the experiments were carried out at $I = 0{\cdot}2$, for which $f_\pm$ has been taken as 0·778 (the value for 0·2M-perchloric acid) while ϕ is estimated as 2·0. Some experiments (not recorded) in which the ionic strength was varied by adding sodium nitrate or sodium perchlorate showed little variation in the observed velocity constant. This finding is difficult to interpret quantitatively, since the observed salt effect is compounded of the effect on three velocity constants and two equilibria.

The most detailed study was carried out with *m*-nitrophenol, which had been previously investigated by Bell and Spencer,[2] the limiting current at a rotating platinum cathode being used to follow the disappearance of bromine. Although introduction of the first bromine lowers the reactivity towards further substitution, the resulting monobromo-derivative is a stronger acid than the original phenol and is therefore present to a larger extent as the highly reactive anion: thus Bell and Spencer had to make a correction of up to 15% for dibromination, although only a few per cent of the phenol was brominated. The greater sensitivity of the method employed here made it possible to use much lower bromine concentrations, the initial concentrations being normally 10^{-3}M-*m*-nitrophenol and 5×10^{-6}M-bromine. Under these conditions the correction for further bromination does not exceed 5% even at the lowest acidities, and the velocity constants given in Table 4 have been corrected in this way. The interpretation of the present results is further simplified by the use of a constant ionic strength $I = 0{\cdot}2$ in place of the high and varying values of I studied by Bell and Spencer.

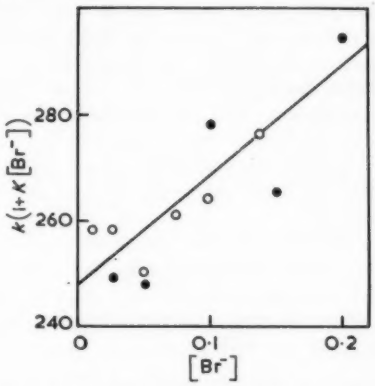
It also appears that the correction for dibromination was not correctly applied by Bell and

[8] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Son, London 1953, Chapter VII.

[9] Wilson and Soper, *J.*, 1949, 3376.

Spencer. Relying on an early paper [10] they assumed that the first product of bromination was a bromonitrophenol of m. p. 147°, assumed to be 2-bromo-3-nitrophenol. More recent work [3] shows that this compound (actually 4-bromo-3-nitrophenol) is formed from bromine vapour and *m*-nitrophenol at high temperatures, but that reaction in acetic acid solution (which more closely resembles our conditions) produces 2-bromo-5-nitrophenol, m. p. 120°. The correction for dibromination ought therefore to be based on measurements with the last compound: the point is unimportant in the present work, but makes an appreciable difference to some of the results of Bell and Spencer. Corrections on this basis have been applied to their results in 0·06M-perchloric acid and are compared with our own data in the Figure, which also serves to show the degree of reproducibility. It is clear that the two different electrical methods lead to substantially the same velocity constants.

Bromination of m-*nitrophenol.*
○, *Results from this paper.*
●, *Bell and Spencer's results (corrected).*



Our results for *m*-nitrophenol are given in Table 4, each being the mean of 2—4 experiments. The calculated velocity constants are from equation (4), with $K = 16$, $K_a = 3{\cdot}98 \times 10^{-9}$ (ref. 11), $\phi = 2{\cdot}0$, $f_{\pm} = 0{\cdot}778$, $k_1 = 101$, $k_2 = 1{\cdot}32 \times 10^9$, $k_3 = 2{\cdot}8 \times 10^7$.

The other phenols were studied less extensively, and only the velocity constants are given in Table 5. The three disubstituted phenols will give, with one molecule of bromine, products

TABLE 4. *Bromination of* m-*nitrophenol at* 25°.

$[HClO_4]$	0·0195	0·0195	0·0195	0·0195	0·0293	0·0293	0·0586	0·0586
$[Br^-]$	0·0494	0·0981	0·147	0·176	0·0494	0·166	0·0104	0·0250
k obs.	301	230	173	165	228	116	220	184
k calc.	309	222	175	160	225	117	214	185
$[HClO_4]$	0·0586	0·0586	0·0586	0·0586	0·146	0·146	0·146	0·146
$[Br^-]$	0·0494	0·0738	0·0981	0·137	0·0104	0·0250	0·0299	0·0494
k obs.	140	120	103	87	138	105	114	85
k calc.	141	117	100	82	137	114	115	88

TABLE 5. *Bromination of various phenols at* 25°.

Compound	K_a	Ref.	k_1	k_2	k_3	k_3/k_2
Phenol	$1{\cdot}1 \times 10^{-10}$	13	$1{\cdot}8 \times 10^5$	—	—	—
p-Bromophenol	$4{\cdot}6 \times 10^{-10}$	14	$3{\cdot}2 \times 10^9$	$7{\cdot}8 \times 10^9$	—	—
2,4-Dibromophenol	$1{\cdot}6 \times 10^{-8}$	*	$5{\cdot}5 \times 10^8$	$1{\cdot}5 \times 10^9$	$5{\cdot}0 \times 10^7$	0·033
m-Nitrophenol	$4{\cdot}0 \times 10^{-9}$	11	$1{\cdot}0 \times 10^8$	$1{\cdot}3 \times 10^9$	$2{\cdot}8 \times 10^7$	0·022
2,6-Dinitrophenol	$1{\cdot}8 \times 10^{-4}$	15	—	$5{\cdot}4 \times 10^6$	$1{\cdot}0 \times 10^5$	0·018
2,4-Dinitrophenol	$8{\cdot}4 \times 10^{-5}$	16	—	$1{\cdot}0 \times 10^8$	$1{\cdot}3 \times 10^4$	0·013

* This value is estimated from $K_a = 1{\cdot}4 \times 10^{-8}$ for 2,4-dichlorophenol.[17]

[10] Linden, *Ber.*, 1885, **18**, 612.
[11] Biggs, *Trans. Faraday Soc.*, 1956, **52**, 35.
[12] Pope and Wood, *J.*, 1912, **101**, 1824.
[13] Hahn and Klockmann, *Z. physikal. Chem.*, 1931, *A*, **157**, 206.
[14] Bordwell and Cooper, *J. Amer. Chem. Soc.*, 1952, **74**, 1058.
[15] Kertes, *J.*, 1955, 1386.
[16] Bale and Monk, *Trans. Faraday Soc.*, 1957, **53**, 450.
[17] Judson and Kilpatrick, *J. Amer. Chem. Soc.*, 1949, **71**, 3115.

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substituted in the 2-, 4-, and 6-positions and therefore will not be brominated further. *p*-Bromophenol gives 2,4-dibromophenol as its first bromination product,[12] but the results for this compound were not sufficiently accurate to justify a correction for further bromination. *p*-Bromophenol is such a weak acid that most of the bromination velocity involves the undissociated molecule, and no estimate of k_3 could be made. With phenol itself the reaction is so fast even in strongly acid solution that neither k_2 nor k_3 could be measured, and the value of k_1 is of low accuracy. The two dinitrophenols are acids of considerable strength, and even in acid solutions only bromination of the anion can be detected.

Discussion

The results for the substituted anisoles (Table 3) show the expected deactivating effect of the electronegative *ortho*- and *meta*-substituents. Substitution in the *para*-position has a much greater effect, since it blocks the favoured position of bromination. The very large deactivating effect of an *o*-nitro-group is of course due to its mesomeric effect, which can stabilize the initial state, but not the transition state in bromination. No bromination by tribromide ion could be detected in any of these reactions, though because of the large salt effects a low reactivity would not have been established with certainty. The results for the bromination of phenols suggest that the most reactive anisoles might be about 1% as reactive towards tribromide ion as towards molecular bromine, which would escape detection.

The same deactivating substituent effects are observed in the bromination of both phenol molecules and phenoxide ions (Table 5). The latter also react detectably with tribromide ion, and although the velocity constants for this reaction are not accurately known, there is good evidence that the reactivity of tribromide relative to molecular bromine increases with increasing reactivity of the organic substance.

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Physical Chemistry Laboratory, Oxford. [*Received, July 18th*, 1960.]

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14. *The Reaction between Aromatic Compounds and Derivatives of Tertiary Acids. Part XII.* Friedel–Crafts Reactions of Camphoric Anhydride in Anisole and in Benzene.*

By William Bleazard and Eugene Rothstein.

The structure of the ketone resulting from the condensation of camphoric anhydride with anisole has been determined by the examination of the optical activities of the further condensation products.

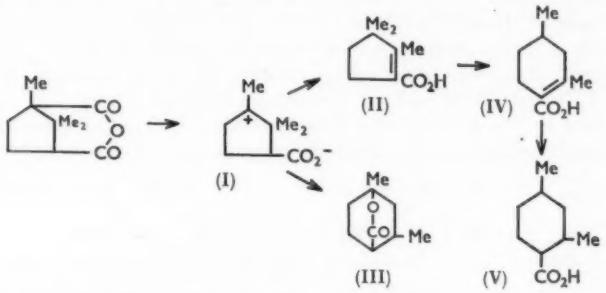
" Phenylcamphoric acid " which is obtained by a similar condensation with benzene, and the phenylated acid produced when isolauronolic acid is also condensed with benzene, may be geometrical isomers. Possible structures for them are discussed.

Condensations of camphoric anhydride with anisole and with benzene were described at the beginning of this century but the orientations of the products have not hitherto been satisfactorily determined. This is partly because the carbonyl group located on the tertiary carbon atom is often eliminated and the resulting carbonium ion (I) may rearrange to form isolauronolic acid (II) or give ring-expansion products such as the lactone (III) of 4-hydroxy-2,4-dimethylcyclohexanecarboxylic acid. Moreover, isolauronolic acid itself is slowly converted by aluminium chloride into 2,4-dimethylcyclohex-1-enecarboxylic acid (IV) or its dihydro-derivative (V).[1]

* Part XI, *J.*, 1958, 3789.

[1] Lees and Perkin, *J.*, 1901, **79**, 356; Perkin and Yates, *ibid.*, p. 1373.

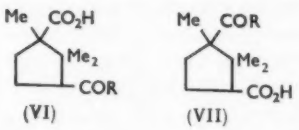
The foregoing rearrangements do not occur when ketones are formed because in these cases the carbonyl group is not eliminated and in consequence the structure of the products is more easily determined. The condensation of camphoric anhydride with anisole, first examined by Eykman [2] and subsequently by Rothstein and Saville,[3] yielded a ketone



which was thought to be either (VI) or (VII) (R = C_6H_4·OMe), but there was no attempt to distinguish between them. This was the case with the similar condensation with toluene but it appeared probable that the results of the anisole reaction would be directly applicable to those of toluene.

Consideration of analogous condensations with dibasic acid anhydrides showed that only the alkylated succinic anhydrides had been examined at all systematically [4] and in these cases electrophilic substitution into benzene was almost invariably by the carbonyl group attached to the least alkylated carbon atom. Although later experiments with substituted glutaric anhydrides carried out by Rothstein and Schofield [5] show that these compounds, which camphoric anhydride resembles in many respects, do not behave in altogether the same way as the lower homologue, the indication was that the ketones had the structure (VI) rather than (VII). The correctness of these conclusions has now been confirmed by examining the optical rotation of the initially formed ketonic acid (VI) and of the products which the further reactions of the latter compound afford.

It was shown in Part XI [6] that retention of optical activity in the Friedel–Crafts synthesis of ketones was associated with derivatives of tertiary acids only; in other cases racemization invariably occurred. In the present case, the substance is an anhydride of both a secondary and a tertiary acid and in consequence optical activity should be retained in any reaction which left the substituents on the tertiary carbon atom undisturbed. The condensation of (−)-camphoric anhydride with anisole yielded a ketonic acid (VI) which was optically active; Clemmensen reduction afforded an optically active acid (VIII) and the acid chloride of this in turn condensed with anisole to give an optically



active ketone (IX). These reactions did not in themselves provide evidence in favour of either of the structures (VI) and (VII), but they did show that optical stability was preserved under fairly vigorous conditions. Clearly, the reaction at the secondary carboxyl residue would destroy the asymmetry of the adjacent carbon atom, but the molecule as a whole

[2] Eykman, *Chem. Weekblad*, 1907, **4**, 727.
[3] Rothstein and Saville, *J.*, 1949, 1961.
[4] Rothstein and Saboor, *J.*, 1943, 425.
[5] Rothstein and Schofield, unpublished work.
[6] Bleazard and Rothstein, *J.*, 1958, 425.

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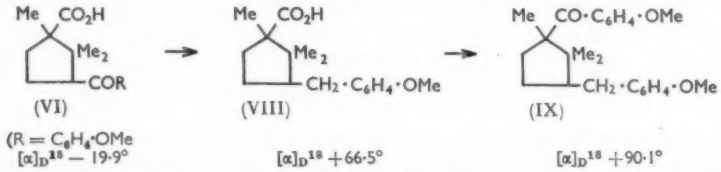
would still be optically active because of the undisturbed asymmetric tertiary carbon atom carrying the other carboxyl group. On the other hand, ketone formation at the tertiary carboxyl residue would not affect the optical activity of the carbon atom to which it was attached though in all probability the catalyst would racemize the other active carbon atom during the reaction. Experimentally it was found that a mixture of the optically active acid chloride of the acid (VIII) in benzene solution with aluminium chloride evolved carbon monoxide with the formation of an optically inactive product. This proved that the chlorocarbonyl group was attached to the optically active tertiary carbon atom and that the acids (VI) and (VIII) had the structures suggested above.

It is necessary to consider whether these heavily alkylated cyclopentane derivatives might not eliminate carbon monoxide by decomposition of the secondary chlorocarbonyl



group. This so far has been encountered mainly with aromatic acid derivatives [3] but otherwise there has not been any systematic investigation of this possibility. Analogy with the examples cited below indicates that the acid chloride, (X; CN replaced by $CH_2{\cdot}C_6H_4{\cdot}OMe$) would yield the corresponding ketone (XI; CN replaced by $CH_2{\cdot}C_6H_4{\cdot}OMe$). Thus the nitrile (X), prepared by unambiguous methods, afforded the ketone (XI) whilst the isomeric compound (XII) eliminated carbon monoxide correspondingly to the acid chloride of (VIII); [7] and similarly, dihydroisolauronoyl chloride yielded 3-benzoyl-1,1,2-trimethylcyclopentane.[8]

The elimination of carbon monoxide from the acid chloride of (VIII) was not accompanied by condensation with benzene, and in this respect it differed from the corresponding reaction of (XII). The structure of the product was not definitely ascertained but it appeared to be either (XIII) or (XIV). Intense infrared absorption at 1625 cm.$^{-1}$ together with the C–H deformation absorption at 849 cm.$^{-1}$ suggested the cyclopentyl olefin (XIV), but its resistance to catalytic hydrogenation indicated a tetrasubstituted ethylenic bond. This resistance to reduction was a major obstacle to the identification of the compound, because the ketone (XV) obtained by condensing isolauronoyl chloride with anisole, gave on reduction, not the methoxybenzyl derivative (XIII), but the dihydro-compound which also resulted from a Clemmensen reduction of the condensation product of dihydroisolauronoyl chloride with anisole.

The structure of " phenylcamphoric acid " obtained in the Friedel–Crafts condensation of camphoric anhydride with benzene has been re-examined. The substance, m. p. 140°, first prepared by Burcker [9] was considered to be 2,2,3-trimethyl-3-phenylcyclopentanecarboxylic acid (XVI), the tertiary carbonyl group having been replaced by phenyl. We have now found the substance to be optically inactive so that there is no doubt that this carbonyl group has been eliminated. No real evidence is available about the position of the phenyl group. It could be on the 3-position as in (XVI) but equally, if a primary rearrangement to the isolauronolic acid structure preceded combination with benzene, it might be either of the acids (XVII) and (XVIII). Other structures derived from the xylic acids (*e.g.*, IV) are also possible. It can be assumed, however, that structure (XVIII) and others with a tertiary acid group are improbable because their acid chlorides would almost certainly lose their carbonyl group in a Friedel–Crafts reaction. We have, on the

[7] Salmon-Legagneur, *Ann. Chim.* (*France*), 1927, **8**, 5.
[8] Shive, Horeczy, and Lochte, *J. Amer. Chem. Soc.*, 1940, **62**, 2744.
[9] Burcker, *Bull. Soc. chim. France*, 1895, **13**, 901.

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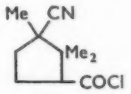
contrary, obtained ketones both in benzene and in anisole solution. The elimination of carbon monoxide from the acid chloride (XII), to which reference has already been made, affords in benzene solution the nitrile which on hydrolysis gives " phenylcamphoric acid " [7] but this has little bearing on its structure because in chloroform rearrangement of the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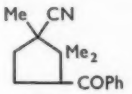
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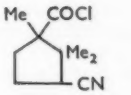
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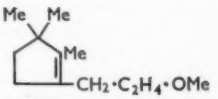
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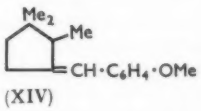
chloride (XII) to isolauronolonitrile accompanied by loss of carbon monoxide occurs [10] and so is analogous to the corresponding reaction of camphoric anhydride.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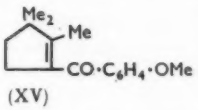
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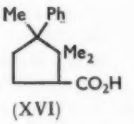
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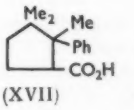
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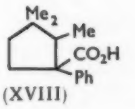
(XVIII)

It was reported by Eykman [2] that isolauronolic acid itself undergoes a slow aluminium chloride-catalysed reaction with benzene, yielding a phenylated acid, m. p. 119°, isomeric with " phenylcamphoric acid," m. p. 140°. His suggested structure was (XVII) for the new acid, and therefore (XVI) for the acid, m. p. 140°. This seemed very likely, provided that the acid, m. p. 119°, had the structure assigned to it, and this could easily be tested by carrying out a Friedel–Crafts condensation with its acid chloride. When the preparation of this acid was repeated, it became evident that it was possibly a geometrical isomer of the acid, m. p. 140°, since a mixture of the two had an intermediate melting point, whilst their infrared spectra were all but identical. The respective acid chlorides condensed with benzene to furnish ketones which differed by 6° in their melting points and also gave an intermediate melting point when mixed. The infrared absorption spectra were again virtually identical. The identity of the two " phenylcamphoric acids " as regards their main skeletal structure necessitates the conclusion that rearrangements of the camphoric, the isolauronolic, or both structures had taken place.

Experimental

Optical rotations were measured for chloroform solutions with $l = 1$, and $c = 2{\cdot}5$. The aluminium chloride was either prepared from aluminium foil or was " free flowing " aluminium chloride supplied by Messrs. British Drug Houses.

Condensations based on (−)-Camphoric Anhydride.—Camphoric anhydride and anisole. Aluminium chloride (45 g.) was slowly added to a stirred solution of (−)-camphoric anhydride (30 g.) in anisole (200 c.c.). Stirring was continued for 2 hr. during which a brilliant red colour developed; then the mixture was decomposed with ice and dilute sulphuric acid and extracted with ether, and the extract in turn extracted with dilute hydroxide solution. Acidification afforded (−)-3-p-*anisoyl*-1,2,2-*trimethylcyclopentanecarboxylic acid* (30 g., 60%), m. p. 178° (from benzene), $[\alpha]_D^{18}$ −19·9° [this m. p. was considerably higher than that found by Rothstein and Saville [3] (165°) for the inactive isomer, but there was no depression of the m. p. when the two were mixed] (Found: C, 70·4; H, 7·6. $C_{17}H_{22}O_4$ requires C, 70·3; H, 7·6%). Clemmensen reduction of the above acid yielded (+)-3-4′-*methoxybenzyl*-1,2,2-*trimethylcyclopentanecarboxylic acid* (VIII), m. p. 133° (from aqueous methanol), $[\alpha]_D^{18}$ +66·5°, in 90% yield (Found: C, 73·8; H, 8·7. $C_{17}H_{24}O_3$ requires C, 73·9; H, 8·7%). Here again large variations in the m. p. indicated the presence of a geometrical isomer. A sample obtained by alkaline hydrolysis of the methyl ester had m. p. 173° and gave an intermediate m. p. when mixed with the lower-melting isomer (Found: C, 74·0; H, 8·8%). The infrared spectra were practically identical.

[10] Salmon-Legagneur, *Compt. rend.*, 1935, **200**, 1222.

XUM

Excess of thionyl chloride at room temperature yielded the acid chloride (70%), b. p. 168—169°/0·3 mm.

Condensation of the acid chloride of (VIII) *with anisole.* The reaction was carried out at room temperature with a solution of the acid chloride (2 g.) in anisole (50 c.c.) and aluminium chloride (2 g.). No carbon monoxide was evolved, and the product, (+)-1-p-*anisoyl*-3-4′-*methoxybenzyl*-1,2,2-*trimethylcyclopentane* (IX), b. p. 180°/0·5 mm. (yield, 1·5 g.), crystallised. Recrystallisation from ethanol gave the ketone, m. p. 96°, $[\alpha]_D^{18}$ +90·1° (Found: C, 78·8; H, 8·4. $C_{24}H_{30}O_2$ requires C, 78·7; H, 8·2%).

Condensation of the acid chloride of (VIII) *with benzene.* A solution of the acid chloride (4 g.) in benzene (10 c.c.) was slowly added to a stirred suspension of aluminium chloride (3 g.) in benzene (40 c.c.) at room temperature. Carbon monoxide (200 c.c., 85%) was evolved and the liquid became deep maroon in colour. After 2 hr. it was decomposed as usual. The *product*, either 1-4′-methoxybenzyl-2,3,3-trimethylcyclopentene (XIII) or 3-4′-methoxybenzylidene-1,1,2-trimethylcyclopentane (XIV), had b. p. 112°/0·4 mm. (Found: C, 83·6; H, 9·6. $C_{16}H_{22}O$ requires C, 83·5; H, 9·6%). It was optically inactive. Aqueous permanganate and bromine water were decolorised by the substance which was, however, unchanged when shaken at room temperature with hydrogen in the presence of 5% palladium–charcoal. Use of platinum oxide catalyst in glacial acetic acid at 5 atm. yielded a mixture of three fractions which could not be identified: (i) b. p. 85—86°/0·11 mm. (Found: C, 74·6; H, 10·7%); (ii) b. p. 94°/0·11 mm. (Found: C, 81·8; H, 10·9%); and (iii) b. p. 110°/0·11 mm. (Found: C, 81·7; H, 10·4%).

Camphoric anhydride and benzene. Under the same reaction conditions as with anisole, carbon monoxide was evolved, and the phenyl derivative, " phenylcamphoric acid," m. p. 139—140° (yield, 70%), was obtained (Found: C, 77·4; H, 8·7. Calc. for $C_{15}H_{20}O_3$: C, 77·6; H, 8·6%). It was optically inactive. Reaction with cold thionyl chloride afforded the acid chloride, b. p. 107°/0·05 mm. (85%), which slowly crystallised.

Condensation of " phenylcamphoroyl chloride " with anisole. Aluminium chloride (10 g.) was added in small portions to a vigorously stirred solution of the acid chloride (16 g.) in anisole (100 c.c.). Carbon monoxide was not evolved and the usual deep-red colour developed. The resulting p-*methoxyphenyl ketone* (3-*p*-anisoyl-1,1,2-trimethyl-2-phenylcyclopentane?) separated from ethanol and had m. p. 151° (yield, 16 g., 78%) (Found: C, 81·5; H, 7·9. $C_{22}H_{26}O_2$ requires C, 82·0; H, 8·1%). The ketone (10 g.) was reduced by amalgamated zinc and hydrochloric acid to the corresponding 4-*methoxybenzyl derivative* (3-4′-methoxybenzyl-1,1,2-trimethyl-2-phenylcyclopentane?), b. p. 172°/0·05 mm. (yield, 8 g., 95%) (Found: C, 85·6; H, 9·1. $C_{22}H_{28}O$ requires C, 85·7; H, 9·1%).

Condensation of the acid chloride with benzene. Repetition of the above reaction with benzene in place of anisole afforded a pale yellow liquid which on decomposition yielded the *phenyl ketone* (3-benzoyl-1,1,2-trimethyl-2-phenylcyclopentane?), as a viscous liquid, b. p. 107°/0·05 mm. (yield, 71%). It gradually crystallised and separated from aqueous ethanol as colourless crystals, m. p. 96°. Further recrystallisations from ligroin (b. p. 40—60°) raised the m. p. to 102° (Found: C, 85·8; H, 8·0. $C_{21}H_{24}O$ requires C, 86·3; H, 8·2%).

Condensations Based in Isolauronolic Acid.—Condensation of isolauronoloyl chloride with anisole. The acid chloride, b. p. 89°/0·05 mm., was obtained in 90% yield from the acid and excess of cold thionyl chloride. A solution of it (15 g.) in anisole (15 c.c.) was added to a stirred solution of aluminium chloride (15 g.) in the same solvent (60 c.c.). After 3 hr. the mixture was decomposed and worked up as usual, furnishing 1-p-*anisoyl*-2,3,3-*trimethylcyclopentene*, b. p. 134—135°/0·11 mm. (14 g., 66%) (Found: C, 78·7; H, 8·3. $C_{16}H_{20}O_2$ requires C, 78·7; H, 8·2%). Clemmensen reduction yielded a product (b. p. 98—100°/0·11 mm.; yield, 57%), the infrared spectrum of which showed it to be the benzyl derivative (compare below) but the hydrogen content was too low (Found: C, 83·4; H, 9·2. Calc. for $C_{16}H_{24}O$: C, 82·8; H, 10·3%). It was accompanied by a fraction, the b. p. of which (195—200°/0·10 mm.) indicated that it might be a bimolecular reduction product (Found: C, 83·5; H, 9·8%); the infrared spectrum indicated the presence of a carbonyl group and possibly hydroxyl.

Condensation of dihydrolisolauronoloyl chloride with anisole. Dihydroisolauronolic acid was obtained as an oil, b. p. 81°/0·2 mm., by catalytic reduction (platinum oxide) of isolauronolic acid in alcohol (yield, 65%) (Found: C, 69·7; H, 10·2. Calc. for $C_9H_{16}O_2$: C, 69·2; H, 10·3%). It gave the acid chloride, b. p. 87°/16 mm. (yield, 96·5%), on reaction with cold thionyl chloride. A mixture of the acid chloride (2·7 g.), aluminium chloride (3 g.), and anisole (30 c.c.) was stirred for 2 hr. From this was isolated 3-p-*anisoyl*-1,1,2-*trimethylcyclopentane*, b. p. 122°/0·8

XUM

mm. (3·3 g., 86%) (Found: C, 78·5; H, 9·2. $C_{16}H_{22}O_2$ requires C, 78·1; H, 8·9%). Clemmensen reduction yielded *3-4'-methoxybenzyl-1,1,2-trimethylcyclopentane*, b. p. 110—111°/0·15 mm. (Found: C, 83·0; H, 10·6. $C_{16}H_{24}O$ requires C, 82·8; H, 10·3%).

Condensation of isolauronolic acid with benzene.[2] A mixture of isolauronolic acid (26 g.), benzene (100 c.c.), and aluminium chloride (30 g.) was left at room temperature for a week. The syrupy product was esterified by saturating its methanolic solution with dry hydrogen chloride. Fractionation of the ester yielded *methyl isolauronolate*, b. p. 87°/12 mm. (8 g.) (Found: C, 71·2; H, 9·4. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·5%), and *methyl 2,3,3-trimethyl-2-phenylcyclopentanecarboxylate* (4 g.), b. p. 106°/0·2 mm., prisms, m. p. 94—95° (from aqueous methanol) (Found: C, 78·0; H, 9·0. $C_{16}H_{22}O_2$ requires C, 78·1; H, 8·9%). Hydrolysis with alcoholic potassium hydroxide afforded the corresponding acid, m. p. 117—119° after two recrystallisations from aqueous ethanol (Found: C, 77·3; H, 8·4. Calc. for $C_{15}H_{20}O_2$: C, 77·6; H, 8·6%). Mixtures of this acid with the acid (m. p. 139—140°) obtained from benzene and camphoric anhydride had intermediate m. p. As already mentioned, the infrared spectra (KCl discs) were nearly identical over the whole range (5000—625 cm.$^{-1}$). The acid chloride was left as a crystalline residue when a mixture of the acid and excess of cold thionyl chloride was left overnight and the excess of reagent removed at room temperature in a vacuum.

Condensation of the above acid chloride with benzene. This was carried out with the acid chloride (2·0 g.), benzene (25 c.c.), and aluminium chloride (2 g.). Two products were obtained: (i) a substance, b. p. 115—118°/0·12 mm., which might have been a ketone (infrared absorption at 1678 cm.$^{-1}$) though a satisfactory analysis was not obtained; and (ii) a *ketone* (40%), b. p. 181°/0·12 mm., flat prisms, m. p. 106—108° [from ligroin (b. p. 40—60°)] (Found: C, 86·5; H, 8·3. $C_{21}H_{24}O$ requires C, 86·3; H, 8·2%). The latter substance appears to be a geometrical isomer of the ketone prepared by two successive condensations of camphoric anhydride with benzene.

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15. *Free-radical Phenylation of Phenanthrene.*

By A. L. J. BECKWITH and M. J. THOMPSON.

Phenyl radicals, produced by thermal decomposition of diazoaminobenzene, react with phenanthrene to yield a mixture of phenylphenanthrenes which has been analysed by chromatography on partially acetylated cellulose and by measurement of ultraviolet absorption. The yields of isomeric phenylphenanthrenes are in accord with modern theories of reactivity in aromatic hydrocarbons. The physical properties and ultraviolet absorption spectra of all the phenylphenanthrenes are recorded herein.

RECENT extensive investigations have proved the relative rates of reaction of unsubstituted aromatic hydrocarbons with free radicals to be substantially in accord with earlier predictions.[1] For instance, appropriate maximum or minimum values of free-valency number and localisation energy for alternant hydrocarbons may be correlated with their rates of reaction with methyl,[2-4] trichloromethyl,[3,5] and benzoylperoxy-radicals.[4,6]

[1] Wheland, *J. Amer. Chem. Soc.*, 1942, **64**, 900; Dewar, *ibid.*, 1952, **74**, 3357; Daudel and Daudel, *J. Chem. Phys.*, 1948, **16**, 639; Burkitt, Coulson, and Longuet-Higgins, *Trans. Faraday Soc.*, 1951, **47**, 553.
[2] Coulson, *J.*, 1955, 1435.
[3] Dewar, Mole, and Warford, *J.*, 1956, 3581.
[4] Pullman and Effinger, "Colloque International sur le Calcul des Fonctions d'Onde Moleculaires," C.N.R.S., Paris, 1958, p. 329.
[5] Kooyman and Farenhorst, *Trans. Faraday Soc.*, 1953, **49**, 58.
[6] Turner and Waters, *J.*, 1956, 879.

XUM

Within any one hydrocarbon there should be a similar relation between the relative rates of free-radical substitution at various positions and the respective theoretical indices, but this hypothesis has not yet been tested rigorously, for in most investigations of this type of reaction either no accurate determination of isomer distribution was attempted or one position in the molecule was so reactive as completely to overshadow other positions (*e.g.*, the reaction of anthracene with methyl [7] or phenyl [8] radicals). In those cases where an accurate analysis of the products was carried out (naphthalene with methyl [9] or phenyl radicals [10]) the number of available positions (two) was not sufficient to test the theory adequately.

Phenanthrene, which has five positions available for substitution, provides an ideal substrate for studies of isomer distribution, particularly as the range in reactivity between the most and the least reactive position is predicted to be similar to that between the 1- and the 2-position of naphthalene.

There have been few previous attempts to bring phenanthrene into reaction with free radicals. With benzyl radicals, produced by reaction of di-t-butyl peroxide with toluene, it yielded an unidentified dibenzyl derivative; [11] with the acetoxy-radicals from manganese triacetate it was converted in small yield into 9-acetoxyphenanthrene.[12] Phenanthrene in chlorobenzene was reported [13] not to react with benzoyl peroxide, but 15% of the starting material was not recovered and the yields of carbon dioxide and benzoic acid strongly suggest that some reaction did, in fact, occur.

For our initial experiments diazoaminobenzene was employed as a source of free radicals. Its thermal decomposition produces both phenyl and anilino-radicals; [14] the latter act as acceptors for hydrogen atoms and so minimise the formation of addition products and the tars which may result therefrom. The reaction was carried out by heating diazoaminobenzene with phenanthrene, which was present in considerable excess to eliminate as far as possible the production of disubstituted compounds. It was essential to eliminate anthracene from our phenanthrene owing to the very rapid reaction of the former.

Analysis of the reaction mixture proved very difficult. Considerable quantities or unchanged phenanthrene were removed by distillation under reduced pressure, and aniline and diphenylamine were isolated by extraction with acid. Treatment of the reaction mixture with acid also precipitated a dark amorphous substance, which contained nitrogen and showed NH absorption in the infrared region. Its formation may indicate that anilino-radicals can react directly with suitable aromatic molecules. The determination of the constituents of the hydrocarbon residue required considerable use of chromatography. Adsorption chromatography on alumina yielded two fractions, the first consisting of phenanthrene, and 9- and 1-phenylphenanthrene, and the second of 2- and 3-phenylphenanthrene. The latter fraction was readily separated into its constituents by fractional crystallisation, since the 2- and 3-phenylphenanthrene are the least and the most soluble respectively of all the isomers. In some cases their proportions in the mixtures were also determined by the ultraviolet-spectrographic method of Dewar and Urch.[15]

The chromatographic procedures recently developed by Spotswood,[16] using acetylated cellulose, facilitated the analysis of the fraction containing phenanthrene and 1- and 9-phenylphenanthrene. Identification and quantitative determination were by ultraviolet

[7] Beckwith and Waters, *J.*, 1956, 1108.
[8] Norman and Waters, *J.*, 1958, 167.
[9] Kent and Norman, *J.*, 1959, 1724.
[10] Marshall and Waters, *J.*, 1959, 381; Huisgen and Grashey, *Annalen*, 1957, **607**, 46; Davies, Hey, and Williams, *J.*, 1958, 1878.
[11] Beckwith, D.Phil. Thesis, Oxford, 1956.
[12] Zonis, *Sbornik Statey po obshchei Khim.*, 1953, **2**, 1091; *Chem. Abs.*, 1955, **49**, 5414.
[13] Roitt and Waters, *J.*, 1952, 2695.
[14] Hardie and Thomson, *J.*, 1958, 1286.
[15] Dewar and Urch, *J.*, 1957, 345.
[16] Spotswood, *J. Chromatog.*, 1960, **3**, 101.

absorption measurements. For mixtures of authentic compounds the method was found to be reproducible and accurate. Infrared spectrography could not be applied to the quantitative analysis of the complex mixtures encountered here because of similarity of the spectra of the components, but proved useful for the qualitative identification of the constituents in various fractions. Chromatography on acetylated paper was employed for the same purpose.[17]

The relative yields of phenylphenanthrenes produced in our experiments are shown in Table 1 together with other relevant data. A notable feature is the absence of 4-phenylphenanthrene: evidently the 4-position is too sterically hindered to allow it to be attacked by phenyl radicals. The results show that the reactivities of the positions in phenanthrene towards substitution by phenyl radicals are in the order $9 > 1 > 3 > 2$. The order of reactivities predicted by all the methods of calculation (see Table 1) is $9 > 1 > 3 > 2$. Our analytical techniques, particularly with regard to 2- and 3-phenylphenanthrene, are not sufficiently accurate to allow a quantitative comparison of reactivities with theoretical indices, but superficially it appears that Dewar's " reactivity numbers " [13] are in better agreement with experiment than others listed in Table 1.

TABLE 1. *Relative yields of substitution products, and theoretical indices of reactivity for phenanthrene.*

	Relative yields of substituted phenanthrenes				Theoretical indices of reactivity			
	Phenylation *							
Position	D.A.B.	B.P.	Nitration [19]	Alkylation [20]	$F_{V.B.}$	$F_{M.O.}$	E	R
1–	4·1	4·6	3·9	0·85	0·197	0·450	2·30	1·86
2–	1·0	1·0	1·0	1·0	0·163	0·402	2·50	2·18
3–	1·0	1·3	3·2	1·57	0·172	0·407	2·41	2·04
4–	0	0	0·8	0	0·184	0·440	2·39	1·96
9–	6·7	6·3	5·3	2·0	0·200	0·451	2·30	1·80

* D.A.B., phenylation with diazoaminobenzene; B.P., phenylation with benzoyl peroxide. $F_{V.B.}$, free-valency number calculated by the valency-bond method (Daudel and Daudel, *J. Chem. Phys.*, 1948, **16**, 639); $F_{M.O.}$ and E, free valency number and atom-localisation energy respectively, calculated by the molecular orbital method (Coulson and Daudel, " Dictionary of Values of Molecular Constants," 1955, Vol. II, p. 20); R, Dewar's " reactivity numbers " (ref. 18).

The results reported here may be compared with similar studies of electrophilic substitution in phenanthrene. Nitration of phenanthrene [19] shows an order of reactivities $9 > 1 > 3 > 2$, and the isomer distribution, except for the 3-position, is very close to that for free-radical phenylation. This agreement is in accord with the accepted theory that free-valency numbers and similar numerical magnitudes provide a measure of reactivity towards all types of chemical reagent, both ionic and free-radical, in unsubstituted alternant hydrocarbons. Electrophilic alkylation of phenanthrene with cyclohexyl benzenesulphonate [20] yields isomeric cyclohexylphenanthrenes in the order $9 > 3 > 2 > 1$. It was suggested that this order differed from that predicted theoretically because of the low selectivity of the attacking reagent.[20] However, decrease in the selectivity of an attacking reagent should lower the total range of reactivity rather than change the order,[21] and we therefore suggest that the low reactivity of the 9- and the 1-position (1-naphthalenic) compared with the 2- and the 3-position (2-naphthalenic) may be ascribed to steric hindrance. The high reactivity of the 3-position towards nitration has been similarly explained.[19] Alternatively, the high yields of 2- and 3-cyclohexylphenanthrenes obtained by Rule and Hickinbottom [20] may be due to the fact that the alkylation is not truly irreversible. It is noteworthy that reversible acylation of phenanthrene yields the 2- and the 3-isomer.[22]

[17] Spotswood, *J. Chromatog.*, 1959, **2**, 90.
[18] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3357.
[19] Dewar and Warford, *J.*, 1956, 3570.
[20] Rule and Hickinbottom, *J.*, 1959, 2517.
[21] Brown and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 6292.
[22] Mosettig and van de Kamp, *J. Amer. Chem. Soc.*, 1930, **52**, 3704.

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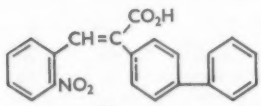
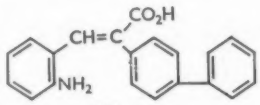
In order to compare diazoaminobenzene as a source of phenyl radicals with the customary reagents, the reaction of phenanthrene with benzoyl peroxide has also been examined. The yield of phenylphenanthrenes from this reaction was low, and the analytical results are accordingly less accurate than those recorded above. Nevertheless, the isomer distribution (Table 1) agrees well with that obtained by using diazoaminobenzene. Though accurate determination of the other reaction products was beyond the scope of this investigation, some points of interest are apparent. The yield of phenols, isolated after hydrolysis of the product mixture, is much greater than that of phenylphenanthrenes, a fact which accords with observations elsewhere [23] that the ratio of benzoyloxylation to phenylation increases with increasing reactivity of the aromatic hydrocarbon. After hydrolysis, the reaction mixture also yielded a neutral gum, insoluble in benzene, which we tentatively suggest is a mixture of dihydrophenanthrenediols, a hypothesis supported by the amount of benzoic acid produced during the hydrolysis. The addition of two benzoyloxy-radicals to an aromatic molecule should be particularly favoured by the presence of two adjacent reactive positions, such as the 9- and the 10-position in phenanthrene.

In order to develop our analytical procedure authentic specimens of all the phenylphenanthrenes were required. 1-, 4-, and 9-Phenylphenanthrenes were prepared by routes similar to those described in the literature, and the 2-isomer was obtained pure from the



(I)



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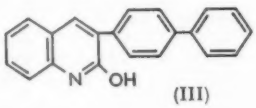

(III)

free-radical phenylation and its identity confirmed by the preparation of derivatives. 3-Phenylphenanthrene,[24] which had not been described when this work was undertaken, was synthesised by Pschorr's method. Condensation of *p*-biphenylylacetic acid with *o*-nitrobenzaldehyde yielded *cis*- and *trans*-α-4-biphenylyl-*o*-nitrocinnamic acid (I). The two isomers, which could be interconverted by irradiation with ultraviolet light, were differentiated by reduction; the *trans*-compound yielded a *trans*-amino-acid (II) whereas the *cis*-isomer was converted into 3-(4-biphenylyl)quinolin-2-ol (III). The quinolinol was

TABLE 2. *Infrared spectra* (μ) *of phenanthrene* * *and phenylphenanthrenes in Nujol*

	Substituted phenanthrenes				
Phenanthrene	1-Phenyl-	2-Phenyl-	3-Phenyl-	4-Phenyl-	9-Phenyl-
10·53s	11·55w	11·21s	11·35s	12·05vs	10·59w
11·45s	11·94w	11·50vw	11·61w	12·50s	11·01vw
11·53s	12·01s	12·26s	12·90vs	12·96w	11·27s
12·25vs	12·35vs	13·46vs	12·50vs	13·13s	11·58w
13·68vs	13·00s	13·81vw	13·16s	13·27s	11·78vw
14·05s	13·15s	14·00w	13·48vs	13·50vs	12·87s
	13·25s	14·45s	14·10vw	13·87vs	13·06s
	13·40s		14·55s	14·30vs	13·50s
	14·18s				13·84s
	14·27s				14·05w
					14·32s

* Anthracene as an impurity in phenanthrene can be detected by its characteristic absorption at 11·25 μ.

also produced by irradiation of *trans*-isomer (II). Cyclisation of acid (II) and decarboxylation of the product yielded 3-phenylphenanthrene.

Ultraviolet spectrographic measurements were extensively used for the qualitative and quantitative analysis of reaction mixtures. The spectra of phenanthrene and 1-, 4-, and

[23] Lynch and Pausacker, *Austral. J. Chem.*, 1957, **10**, 165.
[24] Anderson, Campbell, Leaver, and Stafford, *J.*, 1959, 3992.

XUM

9-phenylphenanthrenes show low-intensity absorption bands of characteristic fine structure, but those of 2- and 3-phenylphenanthrenes are relatively featureless. All the phenylphenanthrenes have characteristic infrared absorption bands and these are recorded in Table 2.

Experimental

Ultraviolet spectra were measured with an Optica Recording Spectrophotometer for solutions in 95% ethanol. Infrared spectra were measured on a Grubb–Parsons S4 double-beam recording spectrophotometer as Nujol mulls with a sodium chloride prism. Analyses were carried out by the C.S.I.R.O. and University of Melbourne Microanalytical Laboratory.

Materials.—Phenanthrene was a commercial sample purified by treatment with maleic anhydride in xylene.[25] It crystallised from ethanol in plates, m. p. 97·5—98°, and then showed ultraviolet absorption almost identical with that of a specimen prepared by the Pschorr method. The synthetic sample had $\lambda_{max.}$ 310, 316, 324, 332, 339, and 346 mμ (ε 172, 209, 236, 288, 242, and 271, respectively). Diazoaminobenzene was purified by chromatography on alumina, and benzoyl peroxide was crystallised from chloroform. Adsorption chromatography was carried out on Spence-type U.G. 1 alumina, with hexane and benzene as eluting solvents.

Chromatography on Partially Acetylated Cellulose.—Cellulose powder was acetylated by Spotswood's method [16] and the quality of the product was tested as follows. The acetylated cellulose was packed in a column 1″ × 12″ with ethanol–toluene–water (17 : 4 : 1), and 2 mg. of an equimolar mixture of perylene and 3,4-benzopyrene were eluted through it with the same solvent mixture until the tail of the perylene band (detected by its fluorescence under ultraviolet light) was 10″ from the top of the column. With satisfactory acetylated cellulose the distance between the tail of the perylene band and the front of the benzopyrene band was then 6·5—7″. Inferior batches, which gave a smaller separation of perylene and benzopyrene, were of no use for the analysis of mixtures of phenylphenanthrenes. For the separation of phenylphenanthrenes the above solvent system was satisfactory but the eluate from the column always showed a weak, featureless, but variable ultraviolet absorption and it was more convenient to use methanol–ether–water (4 : 4 : 1) which gave equally good separation with less background absorption. Mixtures containing phenanthrene and 1- and 9-phenylphenanthrene were separated on a column of acetylated cellulose (1″ × 40″). Constant-volume fractions (7 ml.) were collected and the concentration of hydrocarbon in each tube was determined from the ultraviolet absorption. The intensity at a chosen wavelength was plotted against the tube number, and the area under the curve was obtained by weighing the paper. The percentage composition of the mixture was determined by comparison of these areas after correction by factors derived from the extinction coefficients at the appropriate wavelengths. The total amount of each compound eluted from the column was also determined from the ultraviolet absorption of the combined fractions containing that compound. There was good agreement between results obtained by the two methods. The accuracy of analyses carried out by chromatography on acetylated cellulose was established by test experiments using standard mixtures of pure synthetic hydrocarbons. The most convenient sample size was 12—18 mg. The wavelengths employed for the determination of hydrocarbons in the eluate were phenanthrene, 346 mμ; 1-phenylphenanthrene, 350 mμ; and 9-phenylphenanthrene, 350 mμ.

Reaction of Phenanthrene with Diazoaminobenzene.—An intimate mixture of phenanthrene (200 g.) and diazoaminobenzene (16 g., 0·08 mole) was heated at 152° for 24 hr. There was initially a vigorous evolution of nitrogen, but this ceased after 6 hr. While still molten, the mixture was poured into light petroleum (b. p. 40—60°; 3 l.), and the resultant solution was heated almost to the b. p. and then extracted with hot concentrated hydrochloric acid (2 × 250 ml.). The precipitated tar was collected, washed, and dried, and there was obtained a dark purple solid (3·4 g.), which gave a positive test for nitrogen and ionic chlorine, and showed NH absorption in the infrared spectrum. When the acid extract was evaporated to a small bulk and diluted with water, diphenylamine (0·5 g.) crystallised. It was filtered off and the filtrate was made alkaline and steam-distilled to recover aniline (5·0 g., 66%). The petroleum solution was washed with aqueous alkali, dried, and evaporated. The residual hydrocarbon mixture was distilled under reduced pressure and the distillate (116 g.; b. p. 146—147°/0·5 mm.) was fractionally crystallised from ethanol to yield phenanthrene (113 g., m. p. and

[25] Feldman, Pantages, and Orchin, *J. Amer. Chem. Soc.*, 1951, **73**, 4341.

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mixed m. p. 97—98°) and a mixture (A, 2·7 g.). When the distillation residue was crystallised from light petroleum (500 ml.) a further quantity (45 g.) of substantially pure phenanthrene was obtained. The material dissolved in the mother-liquor was chromatographed on a column (4·5 × 40 cm.) of alumina and eluted with petroleum. The first fraction (4 l.) contained impure phenanthrene (36·5 g.), which was separated by fractional crystallisation from light petroleum into pure phenanthrene (16·7 g.) and a hydrocarbon mixture (B; 5·4 g.). When the mother-liquor and the second chromatographic fraction (11 l.) were combined and evaporated, a mixture (C; 19·8 g.) containing a high proportion of phenylphenanthrenes was obtained. Elution of the column with light petroleum–benzene yielded a mixture (D; 1·9 g.) of 2- and 3-phenylphenanthrene, and a further quantity (1·5 g.) of unidentifiable material was eluted with benzene and ethanol. The mixture (D) was separated into 2- (0·9 g; m. p. 194°) and 3-phenylphenanthrene (0·9 g.; m. p. and mixed m. p. 74°) by fractional crystallisation from ethanol. Mixture (B) was analysed by chromatography on acetylated cellulose (see above) and was found to contain phenanthrene (4·8 g.) and 9- (0·4 g.) and 1-phenylphenanthrene (0·2 g.). A similar determination showed the constituents of (C) to be phenanthrene (10·6 g.) and 9- (5·7 g.) and 1-phenylphenanthrene (3·5 g.). Mixture A contained phenanthrene (1·5 g.) and 9- (0·6 g.), 1- (0·4 g.), 2- (0·1 g.), and 3-phenylphenanthrene (0·1 g.). Yields of phenylphenanthrenes were as follows: 1-, 4·1 g. (0·016 mole); 2-, 1·0 g. (0·004 mole); 3-, 1·0 g. (0·004 mole); and 9-, 6·7 g. (0·026 mole); total yield of phenylphenanthrenes, 12·8 g. (0·05 mole, 62%).

Reaction of Phenanthrene with Benzoyl Peroxide.—Benzoyl peroxide (22·6 g., 0·093 mole) was added slowly (0·5 hr.) to molten phenanthrene (100 g.). During the addition the temperature was allowed to fall from 105° to 90° and it was then kept at 90° for 17 hr.; there appeared to be very little carbon dioxide evolved. The reaction mixture was then dissolved in light petroleum—benzene (1 l.), and the brown solution extracted with aqueous potassium carbonate. Acidification of the aqueous extract yielded benzoic acid (7·3 g.), m. p. 120—121°. The hydrocarbon layer, after drying ($MgSO_4$), was evaporated, and the residue was boiled under reflux with 10% ethanolic potassium hydroxide (300 ml.) for 17 hr. The solvent was removed under reduced pressure, and the residue treated with water (500 ml.) and benzene (1 l.). The aqueous solution was filtered from a gum (9 g.; dihydrophenanthrenediols?) and saturated with carbon dioxide. The phenanthrols (4·5 g., 25%) which were precipitated were extracted with ether. The aqueous solution was then acidified with hydrochloric acid and extracted with ether to yield slightly impure benzoic acid (11·7 g., 0·096 mol.), m. p. 114—118°. The benzene solution was evaporated, and the residue distilled under reduced pressure. The distillate (44·1 g.; b. p. 146—147°/0·5 mm.), on crystallisation from ethanol, yielded pure phenanthrene (40·3 g.). The solvent was removed from the mother-liquor and the residue, combined with that from the distillation, was dissolved in light petroleum and chromatographed on alumina. Thereafter the separation and determination of isomeric phenylphenanthrenes were carried out as described for the earlier experiments. The yields of phenylphenanthrenes were as follows: 1-, 1·4 g. (0·005 mole); 2-, 0·3 g. (0·0012 mole); 3-, 0·4 g. (0·0016 mole); 9-, 1·9 g. (0·0075 mole); total, 4·0 g. (0·016 mole, 17%).

Preparation of Reference Compounds.—1-*Phenylphenanthrene.* γ-1-Naphthyl-γ-oxobutyric acid [26] was reduced by Huang-Minlon's modification of the Wolff–Kishner method [27] to γ-1-naphthylbutyric acid which was cyclised by treatment with phosphorus pentachloride and stannic chloride.[28] The resultant 1,2,3,4-tetrahydro-1-oxophenanthrene (9·7 g.), dissolved in ether, was added to ethereal phenyl-lithium, prepared from bromobenzene (11 g.) and lithium (1 g.), and the mixture was stirred at room temperature for 1·5 hr. then decomposed with ammonium chloride solution. After being washed with water and dried ($MgSO_4$), the ether layer was evaporated, and the residue crystallised from benzene–hexane. 1,2,3,4-Tetrahydro-1-hydroxy-1-phenylphenanthrene (10·7 g., 79%) occurred in prisms, m. p. 112—115° (lit.,[29] m. p. 115—115·5°). When heated under reduced pressure the carbinol was dehydrated to 3,4-dihydro-1-phenylphenanthrene (10·2 g.), b. p. 264°/10 mm., which was fused with sulphur (1·4 g.) at 300° for 1 hr. The crude product was chromatographed in hexane on alumina.

[26] Newman, Taylor, Hodgson, and Garrett, *J. Amer. Chem. Soc.*, 1947, **69**, 1784.
[27] Wilds and Werth, *J. Org. Chem.*, 1952, **17**, 1154; Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487.
[28] Wilds, quoted by W. S. Johnson, *Org. Reactions*, 1944, **2**, 114.
[29] Bachmann and Wilds, *J. Amer. Chem. Soc.*, 1938, **60**, 624.

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Evaporation of the first fractions (4 × 100 ml.) yielded 1-phenylphenanthrene which crystallised from ethanol in needles (7·2 g., 73% from the alcohol), m. p. 79·5—80·5° (lit.,[29] m. p. 79—79·5°), $\lambda_{max.}$ 258, 300, 334, 343, and 350 mμ (ε 60,090, 15,500, 390, 250, and 287 respectively). The *trinitrobenzene complex* crystallised from ethanol in bright yellow needles, m. p. 134—136° with a transition into a second crystal form, m. p. 139—140° (Found: N, 9·1. $C_{26}H_{17}N_3O_6$ requires N, 9·0%). A complex was also obtained with 2,4,7-trinitrofluorenone. When oxidised with chromium trioxide in acetic acid, 1-phenylphenanthrene was converted in good yield into 1-phenylphenanthra-9,10-quinone, orange plates (from acetic acid), m. p. 228° (lit.,[30] m. p. 230—231°) (Found: C, 84·0; H, 4·4. Calc. for $C_{20}H_{12}O_2$: C, 84·5; H, 4·3%).

2-*Phenylphenanthrene*. Because of its strong adsorption on alumina and its relatively low solubility, pure 2-phenylphenanthrene was readily isolated from the free-radical reaction mixture. It crystallised from ethanol in plates, m. p. 194° (lit.,[31] m. p. 196·6—197·2°), $\lambda_{max.}$ 270 (ε 65,700) and 292 mμ (ε 26,000). The trinitrobenzene complex formed yellow plates (from ethanol), m. p. 154·5—155·5° (lit.,[31] m. p. 156—157°), and 2-phenylphenanthraquinone crystallised from acetic acid in deep red plates, m. p. 218° (lit.,[31] m. p. 220—221°).

α-(4-*Biphenylyl*)-o-*nitrocinnamic acid*. 4-Biphenylylacetic acid [32] (7 g.; m. p. 161—162°), triethylamine (4·6 ml.; redistilled), *o*-nitrobenzaldehyde (5 g.), and acetic anhydride (20 ml.) were boiled under reflux for 1·5 hr. The excess of anhydride was decomposed by addition of water (6 ml.) in acetic acid (20 ml.) to the hot reaction mixture, which was then set aside in the refrigerator overnight. The mother-liquor was decanted, and the crude residue (A) washed with acetic acid. The liquors deposited a yellow powder (1·8 g.). The residue (A) was washed with hot toluene to remove a dark brown impurity and then crystallised from acetic acid, a crude product (5·1 g.), m. p. 195—215°, being obtained. When the combined solids were dissolved in a large volume of acetic acid and allowed to crystallise very slowly there was precipitated a mixture of light and dark yellow crystals which were separated by hand-picking. The mother-liquor on slow evaporation yielded further batches of light yellow material. Recrystallisation of the dark yellow material from toluene and from acetic acid yielded prisms (3·6 g., 32%), m. p. 231°, of cis-α-(4-*biphenylyl*)-o-*nitrocinnamic acid* (Found: C, 73·1; H, 4·7; N, 4·0. $C_{21}H_{15}NO_4$ requires C, 73·0; H, 4·4; N, 4·1%), $\lambda_{max.}$ 277 mμ (ε 21,650). The trans-*acid* (3·0 g., 26%) crystallised from toluene or acetic acid in pale yellow prisms, m. p. 231° (Found: C, 72·8; H, 4·5; N, 4·2%); $\lambda_{max.}$ 250 mμ (ε 25,000).

Both isomers when separately irradiated in ethanolic solution with ultraviolet light were converted into the same equilibrium mixture containing mainly the *cis*-acid. In subsequent experiments the two isomers were separated by preparation of the ammonium salts. The salt of the *cis*-acid is readily soluble in water whereas that of the *trans*-acid is relatively insoluble.

trans-o-*Amino*-α-(4-*biphenylyl*)*cinnamic acid*. The foregoing *trans*-nitro-acid (0·95 g.) was dissolved in hot aqueous 0·2N-ammonia (70 ml.), and a solution of ferrous sulphate (7 g.) in water (30 ml.) was stirred in. The mixture was then immersed in a water-bath at 90° and stirred vigorously while concentrated aqueous ammonia (15 ml.) was added dropwise. After 1 hr. the hot solution was filtered through Celite, and the crude product was precipitated by acidification of the cooled filtrate with acetic acid. Further quantities of amino-acid were obtained by extraction of the residue with hot ethanol. The combined solids were purified *via* the ammonium salt, and crystallised from methanol. trans-o-*Amino*-α-(4-*biphenylyl*)-*cinnamic acid* formed pale yellow plates (0·59 g., 68%), m. p. 216—217° (Found: C, 80·0; H, 5·5; N, 4·5. $C_{21}H_{17}NO_2$ requires C, 80·0; H, 5·4; N, 4·4%).

3-(4-*Biphenylyl*)*quinolin*-2-*ol*. (*a*) *cis*-α-(4-Biphenylyl)-*o*-nitrocinnamic acid (0·50 g.) was reduced as above with ferrous sulphate (5 g.) and concentrated aqueous ammonia (13 ml.). After filtration of the mixture the residue was washed with hot water, then dissolved in hot glacial acetic acid containing a drop of sulphuric acid. Dilution of the solution with water yielded the crude product, which was crystallised from acetic acid (charcoal) and from dioxan. The *quinolinol* (0·38 g., 89%) formed needles, m. p. 334° (Found: C, 85·0; H, 5·0; N, 4·6. $C_{21}H_{15}NO$ requires C, 84·8; H, 5·1; N, 4·7%).

(*b*) The quinolinol was precipitated quantitatively when a hot ethanolic solution of the *trans*-amino-acid was irradiated with ultraviolet light.

[30] Fuson and Tomboulian, *J. Amer. Chem. Soc.*, 1957, **79**, 956.
[31] Newman, *J. Org. Chem.*, 1944, **9**, 518.
[32] Long and Henze, *J. Amer. Chem. Soc.*, 1941, **63**, 1939; Schwenk and Papa, *J. Org. Chem.*, 1946, **11**, 798.

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(*c*) *trans-o*-Amino-α-(4-biphenylyl)cinnamic acid (0·15 g.) was refluxed in acetic acid (2 ml.) and sulphuric acid (0·2 ml.) for 1 hr., cooled, and poured into water. Crystallisation of the precipitate from acetic acid yielded pure 3-(4-biphenylyl)quinolin-2-ol (60 mg., 43%), m. p. and mixed m. p. 334°.

3-*Phenyl*-10-*phenanthroic acid*. *trans-o*-Amino-α-(4-biphenylyl)cinnamic acid (1·2 g.) in ethanol (100 ml.) and concentrated hydrochloric acid (2·0 ml.) was stirred at room temperature while isopentyl nitrite (0·6 ml.) was added dropwise. There was a deep yellow coloration, and the formation of the diazonium salt was confirmed by the production of a pink azo-dye with alkaline, aqueous β-naphthol. After 5 min. the solution was treated with copper bronze (2 g.), and there was an immediate evolution of nitrogen. The mixture was warmed to complete the reaction and the product was separated by formation of the soluble sodium salt. 3-*Phenyl*-10-*phenanthroic acid* (1·0 g., 88%), which was precipitated as a white solid, m. p. 233°, by the addition of hydrochloric acid, crystallised from acetic acid in needles, m. p. 235—236° (Found: C, 83·8; H, 4·8. $C_{21}H_{14}O_2$ requires C, 84·5; H, 4·7%).

3-*Phenylphenanthrene*. The foregoing acid (1·1 g.) was refluxed in quinoline (100 ml.) with copper bronze (2 g.) for 1 hr., and the mixture was cooled, diluted with ether, and filtered. The quinoline was removed by extraction with acid, and the crude product isolated by evaporation of the ethereal solution. 3-Phenylphenanthrene (0·85 g., 91%) crystallised from ethanol in long, flat needles, m. p. 70°, raised by recrystallisation to m. p. 76° (lit.,[34] m. p. 73°) (Found: C, 94·4; H, 5·6. Calc. for $C_{20}H_{14}$: C, 94·5; H, 5·5%), $\lambda_{max.}$ 262 (ε 53,900) and 304 mμ (ε 19,700). It formed a *complex* with trinitrobenzene which crystallised from ethanol in orange needles, m. p. 125—126°, with a transition to a second form, m. p. 129—130° (Found: N, 9·1. $C_{26}H_{17}N_3O_6$ requires N, 9·0%). 3-Phenylphenanthraquinone, obtained by oxidation of the hydrocarbon with chromium trioxide in acetic acid, crystallised from acetic acid in yellow needles, m. p. 207—208° (lit.,[34] m. p. 210°) (Found: C, 84·9; H, 4·3. Calc. for $C_{20}H_{12}O_2$: C, 84·5; H, 4·3%).

4-*Phenylphenanthrene*. γ-2-Naphthyl-γ-oxobutyric acid[26,33] was converted into 1,2,3,4-tetrahydro-4-oxophenanthrene as described for the 1-oxo-compound, and 4-phenylphenanthrene was then prepared according to Campbell's method.[34] The product, which was purified by chromatography on alumina, crystallised from ethanol in fine needles, m. p. 80·5—81·5° (lit.,[34] m. p. 80—81°). It had ultraviolet light absorption in ethanol identical with that recorded by Campbell,[34] and formed a complex in ethanol solution with 2,4,7-trinitrofluorenone but not with picric acid or trinitrobenzene. 4-*Phenylphenanthraquinone*, obtained by oxidation of the hydrocarbon with chromium trioxide in acetic acid, crystallised from aqueous acetic acid in orange plates, m. p. 196—197° (Found: C, 84·4; H, 4·4. $C_{20}H_{12}O_2$ requires C, 84·5; H, 4·3%).

9-*Phenylphenanthrene*. A sample of 9-cyclohex-1′-enylphenanthrene (kindly given by Dr. T. M. Spotswood) was dehydrogenated by heating with sulphur. 9-Phenylphenanthrene crystallised from ethanol in plates, m. p. 106°, $\lambda_{max.}$ 257, 288, 299, 335, 343, and 350 mμ (ε 58,700, 12,200, 13,370, 383, 262, and 308, respectively). The *trinitrobenzene complex* crystallised from ethanol in bright yellow needles, m. p. 108·5—109·5° (Found: N, 9·1. $C_{21}H_{17}N_3O_6$ requires N, 9·1%).

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[33] Haworth, *J.*, 1932, 1125.
[34] Campbell, *J.*, 1954, 3659.

16. *Steric Repression of the Mesomeric Effect in Derivatives of* NN-*Dimethylaniline. The Mesomeric Moments of Amino-, Methylamino-, and Dimethylamino-groups.*

By J. W. Smith.

In benzene solution the dipole moments of α-naphthylamine, *NN*-dimethyl-*o*-toluidine, and *NN*-dimethyl-α-naphthylamine are 1·50, 0·95, and 1·06 D, respectively, indicating that in the last two compounds steric repression of the mesomeric effect of the dimethylamino-group must be very strong. The value for *NN*-dimethyl-*o*-toluidine supports the view that in *NN*-dimethylmesidine the axis of the dipole is directed with its negative end away from the aromatic ring.

Evidence regarding the magnitudes of the mesomeric moments in aniline, *N*-methylaniline, and *NN*-dimethylaniline is reviewed and shown to indicate that the vector differences between the moments of these molecules and the " primary dipoles " of the amino-groups are 1·42, 1·66, and 1·69 D, respectively, whilst their components arising solely from the mesomeric effect are about 1·67, 1·93, and 2·06 D, respectively.

As is shown in Table 1, the dipole moments of *NN*-dimethylmesidine and 2,4,6-tribromo-*NN*-dimethylaniline are almost equal and much lower than the dipole moment of *NN*-dimethylaniline, suggesting that the mesomeric effect of the dimethylamino-group may be repressed completely by the steric effects arising in these compounds. On the other hand, the relative values of the dipole moments of *N*-methylaniline, *N*-methylmesidine, 2,4,6-tribromo-*N*-methylaniline, and 2,4-dibromo-*N*-methylaniline suggest that steric inhibition of the mesomeric effect of the methylamino-group is strong in the presence of two *o*-methyl groups, but only slight in the presence of two *o*-bromine atoms and non-existent with only one *o*-bromine atom. These observations were interpreted[1] as indicating that the molecules cannot take up conformations with the *N*-methyl groups near an *o*-methyl or an *o*-bromine atom, or with the amino-hydrogen atom near to an *o*-methyl group. On the other hand, the methylamino-group seems to be able to assume a conformation with the amino-hydrogen atom near an *o*-bromine atom, so that in 2,4,6-tribromo-*N*-methylaniline a conformation is possible which does not permit so great a π-orbital overlap as does the

TABLE 1. *Observed and calculated values of the dipole moments of amines.*

	Unsubstituted		*N*-Methyl		*NN*-Dimethyl	
	Obs. (D)	Calc. (D)	Obs. (D)	Calc. (D)	Obs. (D)	Calc. (D)
Aniline	1·53 [a]	—	1·68 [a]	—	1·61 [a,b]	—
Mesidine	1·45 [a]	1·53	1·22 [a]	1·68	1·03 [d]	1·61
2,4-Xylidine	1·40 [a]	1·45 *	1·54 [a]	1·57 *	0·71 [a]	1·49 *
o-Toluidine	1·59	1·69 *	1·76 [a]	1·86 *	0·96	1·79 *
2,4,6-Tribromoaniline	1·73 [f]	>1·53	1·68 [f]	>1·68	1·02	>1·61
2,4-Dibromoaniline	2·65 [g]	>2·45 *	2·88 [g]	>2·62 *	—	—
α-Naphthylamine	1·50	—	—	—	1·06	~1·58

* Calc. on the basis of free rotation about the N–C bond.
[a] Few and Smith, *J.*, 1949, 753. [b] Everard, Kumar, and Sutton, *J.*, 1951, 2807. [c] Smith, *J.*, 1953, 109. [d] Ingham and Hampson, *J.*, 1939, 981. [e] Fischer, *Acta Chem. Scand.*, 1950, **4**, 1197 Few and Smith, *J.*, 1949, 2663. [g] Smith and Walshaw, *J.*, 1957, 4527.

most favourable conformation of *N*-methylaniline itself, but which nevertheless furnishes appreciable overlap without bringing the *N*-methyl group very near a bromine atom. In *N*-methylmesidine and the trisubstituted *NN*-dimethylanilines the analogous conformations seem to be impossible; so in the latter type of compound the methyl groups must be disposed on opposite sides of the plane of the aromatic ring, thereby making the overlap

[1] Smith and Walshaw, *J.*, 1959, 3784.

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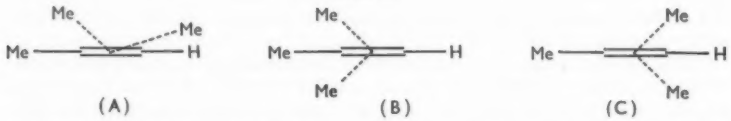
of the lone-pair orbital with the π-orbital system of the ring very small. As an amino-hydrogen atom must be effectively smaller than a *N*-methyl group the repression of the mesomerism, though very strong, may not be quite so complete in *N*-methylmesidine as in *NN*-dimethylmesidine.

If these views are correct it would be expected that the mesomeric effect of the dimethylamino-group would also be strongly sterically inhibited by one obstructive *ortho*-group, such as a methyl group, since at one of the positions of nearest approach of the *o*-methyl and *N*-methyl groups the second *N*-methyl group would be very close to the *o*-hydrogen atom (A, Fig. 1), whilst at the other position the two *N*-methyl groups would

FIG. 1.



be at opposite sides of the plane of the ring (B). In fact, the conformation (C), with both *N*-methyl groups remote from the *o*-methyl group, would be expected to be preferred. In this connexion Wepster [2] has observed that the ultraviolet absorption spectra and relative basic strengths of the amines indicate that the steric inhibition of mesomerism in *NN*-dimethyl-*o*-toluidine is equal to that in *N*-methylmesidine, but less than that in *NN*-dimethylaminodurene. These measurements, however, depend also on the excited states and on the conformations assumed by the $NMeH_2^+$ or NMe_2H^+ groups in the ions, respectively, and it is interesting that his molecular-refraction values appear to show less differences between the steric effects in these compounds.

In view of these facts the dipole moments of *NN*-dimethyl-*o*-toluidine and *NN*-dimethyl-α-naphthylamine have now been determined from measurements on benzene solutions, the values obtained being 0·95 and 1·06 D, respectively. Owing to wide divergencies in the literature, the moment of α-naphthylamine has also been redetermined and found to be 1·50 D. As the dipole moment of aniline is 1·53 D, the dipole moment of *NN*-dimethyl-α-naphthylamine would, in the absence of steric effects, be expected to be only slightly less than that of *NN*-dimethylaniline. The observed value, however, is close to, but slightly higher than, the moment of *NN*-dimethylmesidine, so the evidence suggests that there is very strong, but possibly not quite complete, repression of mesomerism. This is compatible with the chemical evidence afforded by the fact that *NN*-dimethyl-4-nitroso-α-naphthylamine, unlike *NN*-dimethyl-*p*-nitrosoaniline, is unstable.[3]

Steric inhibition of mesomerism must also be strong in *NN*-dimethyl-*o*-toluidine. The dipole moments of toluene (0·37 D), *NN*-dimethylaniline (1·61 D), and *NN*-dimethyl-*p*-toluidine [4] (1·29 D), calculated by Marsden and Sutton's method,[4] indicate that in *NN*-dimethylaniline the angle of inclination of the dipole axis to the 1–4 axis of the ring (θ) is 30°. Similarly, calculation from the moments of *NN*-dimethylaniline and *NNN'N'*-tetramethyl-*p*-phenylenediamine [5] (1·12 D), by use of Williams's equation,[6] indicates [7] that the component of the moment of the former at right angles to the 1–4 axis is 0·79 D, and this leads to $\theta = 29{\cdot}5°$ or 150·5°, of which the former is obviously the value to be accepted. In view of the critical dependence of the derived value of θ upon the exact values of the dipole moments used in the calculations, the agreement between the two methods is remarkably good. If we assume that for *NN*-dimethylaniline $\theta = 29{\cdot}5°$, the

[2] Wepster, *Rec. Trav. chim.*, 1957, **76**, 357.
[3] Gokhlé and Mason, *J.*, 1930, 1757.
[4] Marsden and Sutton, *J.*, 1936, 599.
[5] Everard, Kumar, and Sutton, *J.*, 1951, 2807.
[6] Williams, *Z. phys. Chem.*, 1928, **130**, *A*, 75.
[7] Everard and Sutton, *J.*, 1951, 2818.

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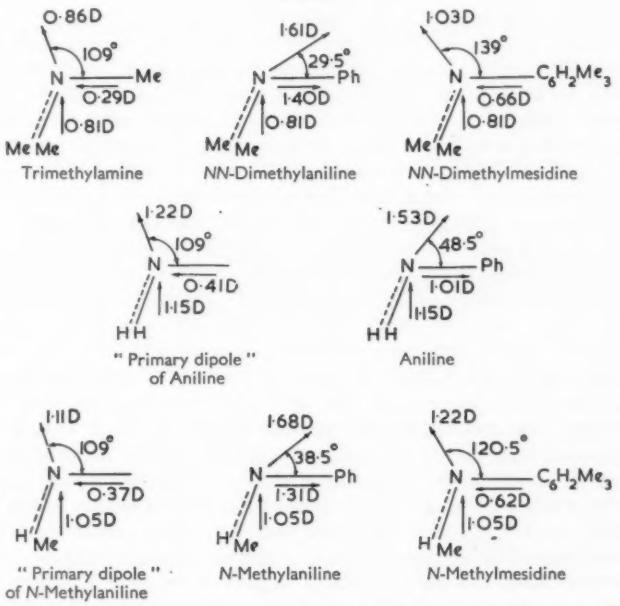
resultant moment of *NN*-dimethyl-*o*-toluidine should be about 1·79 D for free rotation of the dimethylamino-group about the N–C bond or for the conformation in which this group lies as nearly coplanar as possible with the ring. The very much lower observed value indicates strong steric inhibition of mesomerism.

On the assumption that the component of the moment at right angles to the 1–4 axis is the same (0·79 D) in both *NN*-dimethylaniline and *NN*-dimethylmesidine, Everard and Sutton [8] deduced that the component of the dipole moment of the latter compound along the 1–4 axis is ±0·66 D. The dipole moment of *NN*-dimethyl-2,6-xylidine [9] (0·94 D) being less than that of *NN*-dimethylmesidine, the negative value is indicated, showing that for the latter compound $\theta = 139°$. If mesomerism were restricted to the same extent in *NN*-dimethyl-*o*-toluidine as in *NN*-dimethylmesidine, the calculated moments for the conformations B and C (Fig. 1) of the former compound would be 1·21 and 0·67 D,

FIG. 2.



respectively, and that for free rotation about the N–C bond 0·98 D. The observed dipole moment is therefore much nearer the value expected if mesomerism were as restricted as in *NN*-dimethylmesidine than it is to that for no restriction. It is, in fact, compatible with a very strong, but not necessarily complete, restriction of mesomerism, accompanied by a slight preference for the conformation with the methyl groups remote. The experimental value also supports Everard and Sutton's assignment of the sense of the component of the moment of *NN*-dimethylmesidine along the 1–4 axis: if this were +0·66 D, the dipole moment of *NN*-dimethyl-*o*-toluidine should be at least 0·97 D for conformation C and 1·40 D for conformation B.

The present measurements, which indicate that one *ortho*-substituent suppresses the mesomeric effect of the dimethylamino-group strongly, also support the view that in *NN*-dimethylmesidine this effect may be repressed completely. This lends additional weight, therefore, to Everard and Sutton's calculation of the true mesomeric moment in

[8] Everard and Sutton, *J.*, 1951, 2821.
[9] Fischer, *Acta Chem. Scand.*, 1950, **4**, 1197.

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NN-dimethylaniline. The value of this may be deduced rather more simply in the following way. In benzene solution the dipole moment of trimethylamine [10] is 0·86 D, and, since the C–N–C angles are near the tetrahedral value,[11] the components of this moment along and at right angles to one of the N–C bonds, as shown in Fig. 2, are therefore −0·29 and +0·81 D, respectively. The latter is almost equal to the component at right angles to the 1–4 axis in *NN*-dimethylaniline, so the change in moment on passing from trimethylamine to dimethylaniline can be represented by a component of 1·40 + 0·29 = 1·69 D along the 1–4 axis. This will include contributions arising from induction and from the change in type of the carbon orbitals used in the N–C and C–H bonds, as well as from the mesomeric effect. However, if the mesomeric effect is assumed to be repressed completely in *NN*-dimethylmesidine, the difference between the component of its moment along the 1–4 axis (−0·66 D) and that of trimethylamine along an N–C bond (−0·29 D) can be taken as a measure of the first two effects. As a result the true mesomeric moment of *NN*-dimethylaniline appears to be 1·69 + 0·37 = 2·06 D. This confirms the value suggested by Everard and Sutton (2·04 D), but is less than that derived by Ingold [12] on the extreme assumption that the aromatic dimethylamino-group becomes co-planar with the ring.

The corresponding calculation of the mesomeric moment of aniline is not quite so straightforward. In benzene solution the dipole moment of ammonia [10] is 1·45 D, whilst the H–N–H valency angle [11] is about 107°. Hence the components of the moment along and at right angles to one of the N–H bonds are −0·54 and 1·34 D, respectively. If the effective moments of the N–H bonds and their dispositions remained the same in aniline (μ = 1·53 D) as in ammonia, the angle θ for aniline would be $\sin^{-1}$ (1·34/1·53) (= 61°). When this is taken in conjunction with the dipole moment of toluene (0·37 D), the calculated moments of *p*-toluidine, *m*-toluidine, and *p*-phenylenediamine are 1·39, 1·48, and 1·89 D, respectively, whereas the observed values are 1·32, 1·45, and 1·60 D, respectively.[6,13] On the other hand, combination of these experimental moments with those of aniline and toluene leads to angles θ of 49°, 48·5°, and 48°, respectively, with a component to the moment of aniline at right angles to the 1–4 axis of 1·15, 1·15, and 1·14 D, respectively. With some confidence, therefore, θ can be taken as about 48·5°, and the components along and at right angles to the 1–4 axis as 1·01 and 1·15 D, respectively (see Fig. 2). It is apparent, therefore, that the component at right angles to the N–C bond in aniline is reduced, as compared with that at right angles to the N–H bond in ammonia. Nevertheless, if the primary moment is assumed to be directed at the tetrahedral angle to this bond, its value must be about 1·22 D, and its component along the 1–4 axis −0·41 D. The sum of the mesomeric and the inductive moment, and the effects arising from the change in state of hybridisation of the carbon orbitals, is therefore 1·01 + 0·41 = 1·42 D. This is appreciably greater than the value (1·02 D) suggested by Everard and Sutton. The separate contributions from the various effects are difficult to assess, but if, by analogy with the figures for *NN*-dimethylaniline, the sum of the contributions from the inductive effect and from the change in carbon bonding orbitals are taken as −0·25 D, the true mesomeric moment of aniline becomes 1·67 D.

Similarly, from the dipole moments of *N*-methylaniline (1·68 D), *N*-methyl-*p*-toluidine [9] (1·41 D), and toluene it may be deduced that in *N*-methylaniline θ is 38·5°, the components of the moment along and at right angles to the 1–4 axis being 1·31 and 1·05 D, respectively. As the largest contribution to the primary moment must come from the lone-pair orbital, this primary moment may still be taken as being at about the tetrahedral angle to the 1–4 axis, in which case its value must be 1·11 D and its component along the 1–4 axis

[10] Le Fèvre and Russell, *Trans. Faraday Soc.*, 1947, **43**, 374.
[11] Sutton, "Tables of Interatomic Distances and Configurations in Molecules and Ions," Chem. Soc. Spec. Publ. No. 11, 1958.
[12] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, p. 102.
[13] Smith and Walshaw, *J.*, 1957, 4527.

−0·37 D. Hence the sum of the effects due to mesomerism, induction, and change of orbital character comes to 1·31 + 0·37 = 1·68 D. Further, there is evidence that mesomerism is strongly inhibited in *N*-methylmesidine [14] (μ 1·22 D). If the component to the moment at right angles to the 1–4 axis in this compound is the same as in *N*-methylaniline, the component along this bond must be ±0·62 D. No guidance as to which of these values should be taken can be obtained from the moment of *N*-methyl-2,6-xylidine, which has been reported [9] as 1·28 D, whereas the calculated values are 1·44 and 1·08 D, respectively. In view of the undoubtedly strong inhibition of mesomerism in *N*-methylmesidine, however, it seems reasonable to take the component along the 1–4 axis as −0·62 D. It follows, therefore, that the sum of the components arising from induction and change in state of orbital hybridisation must be at least −0·25 D and the true mesomeric moment at least 1·93 D.

Experimental

Materials.—Thiophen-free benzene was purified by repeated crystallisation, followed by drying over sodium.

α-Naphthylamine was distilled twice *in vacuo*, and then crystallised from light petroleum (b. p. 60—80°): it had m. p. 50·0°.

NN-Dimethyl-α-naphthylamine was prepared from α-naphthylamine and dimethyl sulphate by Gokhle and Mason's method [3] and distilled *in vacuo*. It had b. p. 120°/10 mm., n_D^{25} 1·6202, d_4^{25} 1·0377, whence $[R_D]$ = 58·0 c.c. (Perkin [15] gave d_{25}^{25} 1·0391, d_4^{25} 1·0361).

Commercial " pure " *NN*-dimethyl-*o*-toluidine was distilled, the middle fraction (b. p. 184—185°/758 mm.) being used. It had n_D^{25} 1·5240, d_{25}^{25} 0·9238, whence $[R_D]$ = 44·8 c.c. (Ley and Pfeiffer [16] gave b. p. 184·6—185·4/762 mm., n_D^{20} 1·52548, d_4^{25} 0·9287).

Methods and Results.—The solutions were prepared under anhydrous conditions and the dielectric constants (relative to benzene = 2·2741), specific volumes, and refractive indices determined at 25·0° by the method previously described.[17]

Table 2.

α-Naphthylamine				*NN*-Dimethyl-α-naphthylamine			
100*w*	ε	*v*	n_D	100*w*	ε	*v*	n_D
0·0000	2·2741	1·14460	1·4980	0·0000	2·2741	1·14460	1·4980
1·1550	2·2991	1·14145	1·4997	1·3476	2·2875	1·14208	1·4993
1·8302	2·3138	1·13965	1·5007	2·1849	2·2960	1·14050	1·5002
3·1029	2·3420	1·13611	1·5028	3·1932	2·3061	1·13863	1·5012
4·1113	2·3146	1·13336	1·5042	4·8121	2·3220	1·13556	1·5032
				6·4270	2·3376	1·13262	1·5051
				7·2675	2·3457	1·13108	1·5058
α = 2·15, β = −0·2735, γ = 0·453.				α = 1·014, β = −0·1868, γ = 0·319.			
$P_{2\infty}$ = 95·0 c.c., $[R_D]$ = 48·9 c.c.				$P_{2\infty}$ = 81·5 c.c., $[R_D]$ = 58·5 c.c.			
μ = 1·50 D (lit.,[16] 1·44 — 1·53 D).				μ = 1·06 D.			

NN-Dimethyl-*o*-toluidine

100*w*	ε	*v*	n_D	100*w*	ε	*v*	n_D
0·0000	0·2741	1·14460	1·4980	4·5905	2·3087	1·14204	1·4989
1·2794	2·2837	1·14389	1·4982	6·3047	2·3213	1·14104	1·4992
2·9190	2·2960	1·14299	1·4985	8·3296	2·3367	1·13982	1·4996
4·2274	2·3057	1·14222	1·4988				

α = 0·75, β = −0·0564, γ = 0·056.
$P_{2\infty}$ = 62·9 c.c., $[R_D]$ = 44·6 c.c., μ = 0·95 D (Fischer [9] found μ = 0·88 D).

The results are recorded in Table 2, where α, β, and γ indicate the limiting values of dε/d*w*, d*v*/d*w*, and dn^2/d*w*, respectively, at zero concentration, and the other symbols have their usual significance. The dipole moments derived from these data, and the values for other substances referred to in the discussion, are all calculated on the assumption that ${}_\mu P = {}_T P - [R_D]$.

[14] Smith, *J.*, 1953, 109.
[15] Perkin, *J.*, 1895, **69**, 1213.
[16] Ley and Pfeiffer, *Ber.*, 1921, **54**, 363.
[17] Few and Smith, *J.*, 1949, 753.
[18] Wesson, " Tables of Electric Dipole Moments," Technology Press, Cambridge, Mass., 1948.

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The moment now found for α-naphthylamine differs from that of Cowley and Partington [19] principally on account of the different $[R_D]$ value used. The experimental figure (48·9 c.c.) is in agreement with the value calculated by adding the difference between the molar refractions of naphthalene (44·4 c.c.) and benzene (26·2 c.c.) to that of aniline (30·7 c.c.). On the other hand, the experimental values of $[R_D]$ for *NN*-dimethyl-α-naphthylamine and *NN*-dimethyl-*o*-toluidine, whether deduced from the measurements on the solutions or from the properties of the pure liquids, are appreciably less than the values calculated in a similar way from the molar refraction of *NN*-dimethylaniline. This furnishes additional evidence for strong steric inhibition of mesomerism in their molecules.

Thanks are tendered to Imperial Chemical Industries Limited for a grant and for the loan of a precision variable condenser.

BEDFORD COLLEGE, REGENT'S PARK, LONDON, N.W.1. [*Received, May 30th,* 1960.]

[19] Cowley and Partington, *J.*, 1938, 1598.

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17. *Cobalt Phosphates. Part II.*[1] *Phase-diagram Studies of Some Cobalt*(III) *Ammine Phosphates.*

By SALHA S. DANIEL and J. E. SALMON.

Studies of the systems $[Co(NH_3)_6]_2O_3$–P_2O_5–H_2O at 25° and $[Co(NH_3)_5H_2O]_2O_3$–P_2O_5–H_2O at 0° and 25°, have shown a similarity between them which indicates that tervalent cations are present in each.

The diaquotetrammine phosphates behave differently. Their solutions in aqueous phosphoric acid were unstable and the complex decomposed if the phosphoric oxide content was less than 18% and the solutions were too viscous for a solid phase to separate if more than 35% of phosphoric oxide was present. Between these limits a solid phase separated which was best represented by the components $[Co(NH_3)_4(HPO_4)]_2O$–P_2O_5–H_2O, and evidence is presented to show that under these conditions phosphato-tetrammine ions, with a bidentate phosphato-group, are present in both liquid and solid phases.

IN Part I,[1] where previous work on amminecobalt(III) phosphates and amminephosphatocobalt(III) complexes was reviewed, it was shown that, whilst phosphatotetramminecobalt(III) compounds could be separated from aqueous solution, yet all attempts to prepare phosphatopentamminecobalt(III) complexes yielded aquopentamminecobalt(III) phosphates instead. The tetrammine complexes appeared to contain a bidentate phosphate group, which might account for their having greater stability than the pentamine complexes where the phosphate would be present as a unidentate group. Evidently, if such a unidentate group is introduced it is readily displaced by water molecules from the solvent. Hence it seemed of interest to ascertain if the reverse process could be achieved, namely, the displacement of water molecules from the co-ordination sphere by phosphate groups, by the use of concentrated solutions of phosphoric acid.

A convenient method of approach was offered by the study of the systems aquopentamminecobalt(III) oxide–phosphoric oxide–water and the corresponding diaquotetrammine system, from which evidence might be obtained of the stage at which replacement of aquo- by phosphato-groups occurred. The corresponding hexammine system was studied at the same time for comparison. These systems are presumably thermodynamically unstable,[2] but, except for one region of the diagram for the tetrammine system at 25°, metastable states were encountered of sufficient stability for solid phases of definite compositions to persist in contact with solutions for many weeks.

[1] Part I, Daniel and Salmon, *J.*, 1957, 4207.
[2] Taube, *Chem. Rev.*, 1952, **50**, 69.

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Experimental

Starting Materials.—Hexamminecobalt(III) phosphate dihydrate was prepared from the corresponding chloride by a method similar to that used for the aquopentammine phosphate (method no. 3a in Part I [1]). The aquopentammine and diaquotetrammine phosphates were prepared as before: [1] it was unnecessary to purify the *cis*-chloroaquotetramminecobalt(III) sulphate used in the latter preparation.

Phase Diagrams.—The methods used were those of Jameson and Salmon.[2] The solutions of both the aquopentammine and the diaquotetrammine phosphate were prepared at the appropriate temperature by addition, to solutions of phosphoric acid, of portions of the starting material until an undissolved residue remained. With the hexammine phosphate some saturated solutions prepared at 40—50° deposited a solid phase on cooling; otherwise the method just described was used.

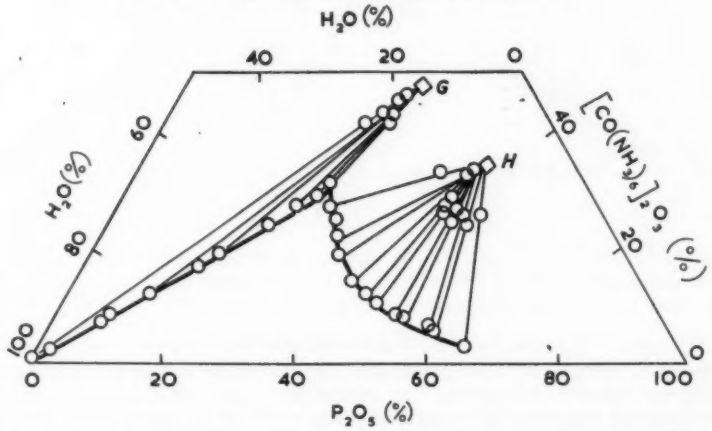
Analytical Methods.—These were described in Part I.[1]

Additional Examination of the Solid Phases.—The solid was freed as completely as possible from the solution adhering to it after filtration, either by washing with water (if the stability of the compound permitted) or by pressing between filter-papers. Solutions of known concentration were then prepared for spectrophotometric and, if possible, conductivity measurements.

Table 1. *System* $[Co(NH_3)_6]_2O_3$–P_2O_5–H_2O *at* 25°.

Solution (%)		Solid (%)		Solution (%)		Solid (%)	
$[Co(NH_3)_6]_2O_3$	P_2O_5	$[Co(NH_3)_6]_2O_3$	P_2O_5	$[Co(NH_3)_6]_2O_3$	P_2O_5	$[Co(NH_3)_6]_2O_3$	P_2O_5
0·663	0·533	40·95	30·80	24·11	34·88	32·25	49·88
2·269	3·036	44·24	33·28	21·24	36·35	32·89	50·92
6·85	8·03	43·68	32·48	18·12	38·60	32·35	50·10
7·95	8·78	43·50	32·88	13·79	42·36	28·67	50·02
11·53	13·01	44·98	33·80	11·85	45·41	27·00	49·60
16·20	18·21	44·23	33·22	9·98	47·90	25·45	50·09
18·50	19·97	42·60	32·51	8·34	51·33	26·41	51·74
23·48	24·90	45·90	34·45	7·68	53·16	23·98	52·23
26·88	27·13	46·00	34·51	6·23	57·71	25·66	53·10
28·46	29·90	42·21	34·12	5·33	58·77	23·46	54·41
30·75	30·62	40·86	34·86	2·60	65·04	25·40	55·94
26·63	32·54	32·74	49·19				

Fig. 1. *The system* $[Co(NH_3)_6]_2O_3$–P_2O_5–H_2O *at* 25°.



Results.—Hexamminecobalt(III) *system.* The following new *compounds* (which for convenience have been designated by letters, following on from Part I) were found as solid phases at 25° (Table 1, Fig. 1): *G* $[Co(NH_3)_6]_2O_3,2P_2O_5,7H_2O$, as orange needles, and

H $[Co(NH_3)_6]_2O_3,4P_2O_5,9H_2O$,

[2] Jameson and Salmon, *J.*, 1954, 4013; 1955, 360.

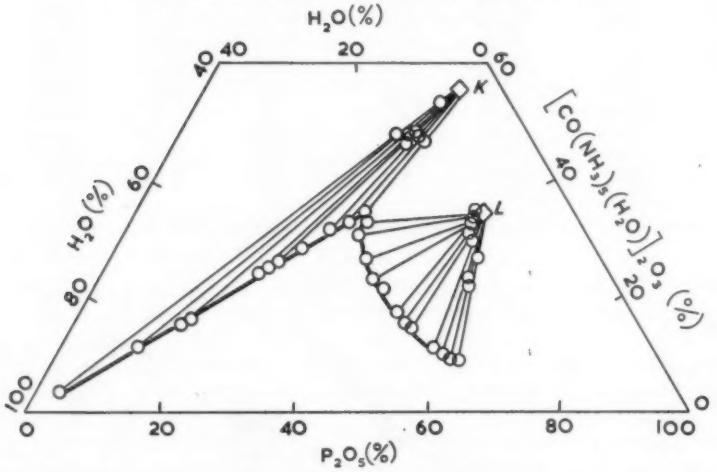
as red, water-soluble crystals which slowly disintegrated on exposure to air. If the solutions which had been in contact with these solid phases were filtered and diluted and the acid present neutralized with aqueous ammonia, a third new *compound*, *J*, separated as fine insoluble orange crystals {Found: Co, 18·2; NH_3, 32·6; PO_4 (total, all ionizable), 44·6. $2[Co(NH_3)_6]_2O_3,3P_2O_5,6H_2O$ requires Co, 18·2; NH_3, 32·1; PO_4, 44·7%}.

Pentamminecobalt(III) *system.* For the range of solutions up to 60% of P_2O_5 at 0° the following new *compounds* were indicated (Table 2, Fig. 2): *K* as fine, insoluble, red crystals

TABLE 2. *System* $[Co(NH_3)_5H_2O]_2O_3$–P_2O_5–H_2O *at* 0°.

Solution (%)		Solid (%)		Solution (%)		Solid (%)	
$[Co(NH_3)_5H_2O]_2O_3$	P_2O_5	$[Co(NH_3)_5H_2O]_2O_3$	P_2O_5	$[Co(NH_3)_5H_2O]_2O_3$	P_2O_5	$[Co(NH_3)_5H_2O]_2O_3$	P_2O_5
3·795	3·59	47·95	32·57	30·41	35·23	33·72	51·38
11·54	11·31	53·11	36·40	26·53	38·48	33·08	51·85
15·21	16·26	36·73	33·42	22·98	41·20	33·86	52·07
16·12	16·70	48·02	35·34	21·31	43·13	33·12	51·42
24·00	23·20	48·14	35·00	17·56	47·32	32·47	51·63
25·10	24·33	48·52	35·35	15·36	49·60	30·62	51·91
26·30	25·48	46·86	34·96	14·21	50·91	31·51	52·03
28·30	27·91	48·40	35·35	11·47	56·00	29·60	52·85
31·40	31·67	46·78	35·01	9·98	57·82	23·13	55·51
32·70	32·68	47·79	36·37	8·87	59·85	21·64	56·10
34·20	34·27	46·72	37·58	8·92	60·97	26·38	55·23
32·88	35·12	33·99	51·72				

FIG. 2. *The system* $[Co(NH_3)_5(H_2O)]_2O_3$–P_2O_5–H_2O *at* 0°.



$5[Co(NH_3)_5H_2O]_2O_3,9P_2O_5,12H_2O$; *L* as large, irregular, red, water-soluble crystals $[Co(NH_3)_5(H_2O)]_2O_3,4P_2O_5,9H_2O$. The latter are unstable when dry.

For the same system at 25° (Table 3, Fig. 3) a new *compound M*,

$$[Co(NH_3)_5H_2O]_2O_3,2P_2O_5,3H_2O$$

and compound *L* were found as solid phases. If, after they had been separated from the solid phases, the supernatant solutions were diluted and an excess of aqueous ammonia added to them crystals of compound *A*[1] separated {Found: Co, 21·3; NH_3, 31·1; PO_4 (total, all ionized), 34·4. Calc. for $[Co(NH_3)_5H_2O]PO_4,H_2O$: Co, 21·4; NH_3, 31·0; PO_4, 34·5%}.

Tetramminecobalt(III) *system.* At 25° decomposition of the tetramminecobalt(III) ion occurred with solutions containing less than 15% of P_2O_5, and no solid could be made to separate from solutions containing more than 35% of P_2O_5. For the solutions in the range 15—35% of P_2O_5 (total) it proved possible to represent the analytical data in terms of the components $3[Co(NH_3)_4(HPO_4)]_2O$–P_2O_5–H_2O (Table 4, Fig. 4) when the dark purple crystals of the solid

phase were identified as compound *N*, $3[Co(NH_3)_4(HPO_4)]_2O,P_2O_5,24H_2O$ (a hydrate of compound *C*, ref. 1), but not in terms of the components $[Co(NH_3)_4(H_2O)_2]_2O_3$–$P_2O_5$–$H_2O$. On addition of dilute aqueous ammonia to solutions which had been in contact with compound *N*, compound *C* was obtained {Found: Co, 23·2; NH_3, 26·85; total PO_4, 49·7; ionized PO_4, 14·0; H_2O, 0·2. Calc. for $[Co(NH_3)_4(HPO_4)]_3PO_4$: Co, 23·1; NH_3, 26·7; total PO_4, 50·1; ionized PO_4, 12·5%}. Addition of dilute aqueous ammonia to the solutions containing over 35% of

TABLE 3. *System* $[Co(NH_3)_5H_2O]_2O_3$–P_2O_5–H_2O *at* 25°.

Solution (%)		Solid (%)		Solution (%)		Solid (%)	
$[Co(NH_3)_5H_2O]_2O_3$	P_2O_5	$[Co(NH_3)_5H_2O]_2O_3$	P_2O_5	$[Co(NH_3)_5H_2O]_2O_3$	P_2O_5	$[Co(NH_3)_5H_2O]_2O_3$	P_2O_5
22·30	22·87	44·91	35·61	34·42	35·60	50·32	39·28
23·07	23·12	29·05	26·29	35·87	37·23	46·29	39·37
23·96	24·34	27·89	26·64	35·67	38·67	36·98	50·12
27·92	27·60	49·02	38·19	29·42	42·09	31·85	49·09
27·84	28·48	48·97	38·21	22·99	47·93	31·93	52·82
29·98	30·30	32·63	31·70	18·21	54·64	31·17	53·79

TABLE 4. *System* $[Co(NH_3)_4HPO_4]_2O$–P_2O_5–H_2O *at* 25°.

Solution (%)		Solid (%)		Solution (%)		Solid (%)	
	Free		Free		Free		Free
$[Co(NH_3)_4HPO_4]_2O$	P_2O_5	$[Co(NH_3)_4HPO_4]_2O$	P_2O_5	$[Co(NH_3)_4HPO_4]_2O$	P_2O_5	$[Co(NH_3)_4HPO_4]_2O$	P_2O_5
56·68	4·11	68·63	6·03	55·74	14·72	67·27	9·21
56·13	5·28	70·94	6·42	56·18	16·88	68·31	9·56
56·72	6·52	65·20	6·51	57·86	17·45	61·11	15·03
55·79	8·43	68·97	2·78	57·35	19·62	64·43	12·18
55·98	8·92	65·83	7·08	58·49	20·83	64·62	13·02
56·68	11·86	69·20	7·31	58·57	22·57	68·07	12·15
55·63	12·66	68·24	8·28				

FIG. 3. *The system* $[Co(NH_3)_5(H_2O)]_2O_3$–P_2O_5–H_2O *at* 25°.

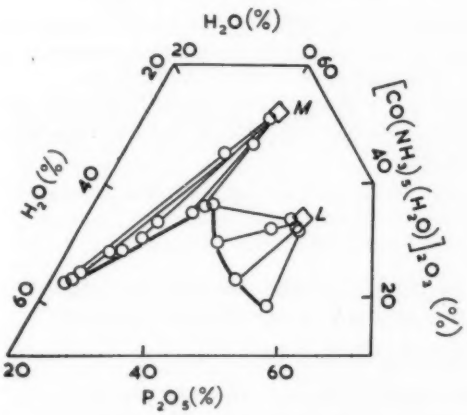
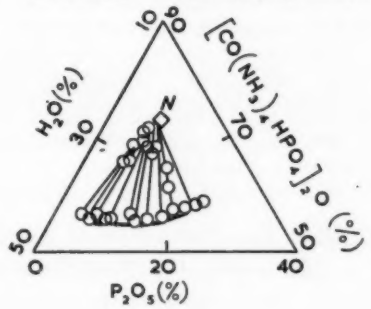


FIG. 4. *The system* $[Co(NH_3)_4(HPO_4)]_2O$–P_2O_5–H_2O *at* 25°.



P_2O_5, from which no solid phase had separated, caused the precipitation of dark purple crystals of a new *compound* P {Found: Co, 19·0; NH_3, 22·4; total PO_4, 46·1; ionized PO_4, 16·6; H_2O, 12·5. $[Co(NH_3)_4(HPO_4)]_2HPO_4,4H_2O$ requires Co, 19·2; NH_3, 22·1; total PO_4, 46·3; ionized PO_4, 15·4; H_2O, 11·7%}; $\Lambda_{2478} = 312$ for *P* indicates the probable presence of 3 ions in solution.

DISCUSSION

The Hexammine- and Pentammine-cobalt(III) *Systems.*—The marked similarity of these two systems (Figs. 1, 2, and 3) and of the solid phases separating from them leads us to infer that in each case the same type of ion (*i.e.*, a tervalent one) is present. The conclusion to

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be drawn is that, in the pentammine system, the ion present is the aquopentamminecobalt(III). Support is provided in the separation from the aqueous phase of this system of the previously known aquopentamminecobalt(III) phosphate (compound *A*, ref. 1) on addition of ammonia to the liquid. The similarity of the absorption spectra of compound *L* and of the aquopentammine phosphate (Table 5) also suggests that the same cation is present in each. It is evident that even at high concentrations of phosphate in solution (*e.g.*, up to 50% of P_2O_5, Tables 1—3) the phosphato-group is unable to displace the aquo-group from the pentammine complex.

The Tetramminecobalt(III) *System.*—This system differed from the other two in that attempts to represent it in terms of the same type of components [*i.e.*, on the assumption that the cation was the diaquotetramminecobalt(III) ion] led to tie lines that crossed irregularly without meeting at any given point. Trial and error showed that it could be satisfactorily represented by using the components $[Co(NH_3)_4(HPO_4)]_2O$,P_2O_5 and H_2O (Fig. 4). This indicates that, as soon as the solutions contain sufficient acid to stabilize the tetrammine ion, the two aquo-groups are displaced by a phosphate group. In support of this, the phosphate tetrammine compounds $[Co(NH_3)_4(HPO_4)]_3PO_4$ (compound *C*, ref. 1) and $[Co(NH_3)_4(HPO_4)]_2HPO_4$ (compound *P*) can be made to separate from aqueous phases of this system. A solution of compound *P* in 12M-phosphoric acid shows the strong peak

TABLE 5. *Absorption spectra for visible and ultraviolet regions.*

Compound	$\lambda_{max.}$	*E*	$\lambda_{max.}$	*E*	$\lambda_{max.}$	*E*
* $[Co(NH_3)_5(H_2O)]_2O_3,4P_2O_5,9H_2O$ (compound *L*)	3450	42	4820	44	—	—
† $[Co(NH_3)_5H_2O]PO_4,2H_2O$ (compound *D*, ref. 1)	3420	43	4850	48	—	—
‡ $[Co(NH_3)_4(HPO_4)]_2HPO_4,4H_2O$ (compound *P*)	§	§	5260	73	6900	33·5
† $[Co(NH_3)_4(PO_4)],2H_2O$ (compound *E*, ref. 1)	3650	23	5220	37	6950	61
* $[Co(NH_3)_4(CO_3)]NO_3$	3500	§	5260	57	7040	26

* Solvent water. † Solvent M/100-H_3PO_4. ‡ Solvent 12M-H_3PO_4. § Not recorded.

at about 6950 Å that characterizes compound *E* ($[Co(NH_3)_4PO_4],2H_2O$, ref. 1) and the carbonatotetrammine ion, but like solutions of compound *C* it is rapidly hydrolyzed in M/100-phosphoric acid, and this peak does not appear in such solutions (Table 5).

Apparently, the ion containing the monohydrogen phosphate ligand $[Co(NH_3)_4(HPO_4)]^+$ is more susceptible to hydrolysis than the neutral complex $[Co(NH_3)_4(PO_4)]$, although there is no very obvious reason why this should be so.

BATTERSEA COLLEGE OF TECHNOLOGY, S.W.11. [*Received, May 30th,* 1960.]

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18. *The Extraction of Nitric Acid from Aqueous Solution by Organic Solvents: the Dimerisation of Nitric Acid in the Organic Solvent.*

By C. J. HARDY, B. F. GREENFIELD, and D. SCARGILL.

The extraction of nitric acid from aqueous solution (6—16M) into benzene and into toluene, and the infrared spectrum of the benzene phase, have been measured. It appears that the nitric acid in the organic phase is present as a monohydrated dimer.

DURING investigations [1] on the extraction of nitric acid from aqueous solution by dialkyl hydrogen phosphates in the diluents toluene, kerosene, n-dodecane, and carbon tetrachloride, it was observed that a little nitric acid is extracted by the diluents alone. As the nature of this extraction appears to be unknown we have examined in greater detail the extraction of nitric acid by toluene and benzene.

[1] Hardy and Greenfield, unpublished work.

Values of C_a and C_o, the equilibrium concentrations of nitric acid in the aqueous and the organic phase respectively, and C_{H_2O}, the equilibrium concentration of water in the toluene phase, are given in Table 1 for certain solvents. The value of $C_{o,\,calc.}$ was calculated from

$$C_o = D \,.\, C_{u,a} + 2KD^2 \,.\, C_{u,a}{}^2$$

in which $C_{u,a}$ is the equilibrium concentration of the un-ionised nitric acid in the aqueous phase (taken from the data of Krawetz kindly made available by Hesford and McKay [2] from their original graphs), D is the distribution coefficient of un-ionised nitric acid between

TABLE 1. *Values of* C_a, $C_{u,a}$, C_o, *and* C_{H_2O}.

Solvent	C_a (M)	$C_{u,a}$ (M) (from ref. 2)	C_o (M) exptl.	C_o (M) calc.	C_{H_2O} (M)	Solvent	C_a (M)	$C_{u,a}$ (M) (from ref. 2)	C_o (M) exptl.	C_o (M) calc.
Toluene	6·16	1·58	0·0062	0·0061		Kerosene ...	9·2	4·05	0·0010	0·0007
	9·20	4·05	0·0334	0·0323			12·2	7·75	0·0020	0·0023
	10·15	5·20	0·0505	0·0518			16·1	—	0·0064	0·0064
	12·10	7·65	0·108	0·108		CCl_4	14·1	10·7	0·0145	
	13·90	10·4	0·210	0·195			16·1	—	0·027	
	13·75	10·1	0·248		0·124	Cyclohexane	12·2	7·75	0·0016	
	15·12	—	0·86		0·425		13·9	10·4	0·0034	
Benzene	14·1	10·7	0·22			n-Dodecane	8·1	3·0	0·034	
	15·6	—	0·47				14·1	10·7	0·080	

TABLE 2. *Infrared difference spectrum of* 0·2M-*nitric acid in benzene against benzene.*

Peak max. (cm.$^{-1}$)	Assignment	Peak max. (cm.$^{-1}$)	Assignment
768w	ν_6 NO_3 out-of-plane	1401m	? NO_3^- ion
894s }	ν_2 NO stretch	1595w	Water H–O–H bend
929s }		1668s	ν_4 NO_2 antisym. stretch
1299vs	ν_1 NO_2 sym. stretch	2703w	? combination band
~1340 *	ν_5 H-bend	3215m }	ν_7 OH stretch
		3495w }	
		3571m }	

* Shoulder on 1299 band.

the two phases ($C_{u,o}/C_{u,a}$), and K is the stoicheiometric equilibrium constant given by $[(HNO_3)_2]_o/[HNO_3]_{u,o}{}^2$ for the equilibrium $2HNO_{3u,o} \rightleftharpoons (HNO_3)_{2,o}$. Values of $D = 1{\cdot}2 \times 10^{-3}$, and $K = 590$ mole^{-1}, were derived for this equation from the plot of $C_o \,.\, C_{u,a}{}^{-1}$ against $C_{u,a}$, a straight line of slope $2KD^2$ with intercept D at $C_{u,a} = 0$.

Similar calculations on the results for kerosene give approximately $D = 6 \times 10^{-5}$ and $K = 4 \times 10^3$ mole^{-1}, which were inserted in the equation to obtain the values of $C_{o,calc.}$ in Table 1.

The frequencies and intensities of the bands in the infrared difference spectrum between benzene, and of benzene containing 0·2M-nitric acid (extracted from 14M-nitric acid), are given in Table 2. Similar results were obtained in carbon tetrachloride and n-dodecane. The assignments of the frequencies of the bands due to the nitric acid molecule are those of Cohn, Ingold, and Poole.[3] The spectrum was not measured in toluene because significant attack on the toluene would have occurred during the measurements.

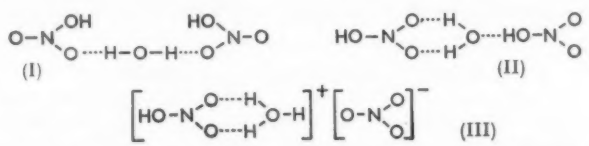
DISCUSSION

The above evidence strongly supports the idea that a dimer of nitric acid is the predominant species in solvents such as toluene, benzene, and kerosene, in contact with aqueous nitric acid under the range of conditions studied. Since the molar concentration of water in the toluene phase is approximately one-half the molar concentration of nitric acid in that phase, the dimer probably exists as the monohydrate, $(HNO_3)_2,H_2O$. This

[2] Hesford and McKay, *Trans. Faraday Soc.*, 1958, **54**, 573.
[3] Cohn, Ingold, and Poole, *J.*, 1952, 4272.

composition is the same as that of the hemihydrate of nitric acid found by Erdmann [4] and confirmed by Chédin [5] in an aqueous nitric acid containing >90% of HNO_3, and also postulated by Gillespie, Hughes, and Ingold [6] to interpret their freezing point results for >95% HNO_3.

The infrared spectrum of the $(HNO_3)_2,H_2O$ species in benzene has the interesting features (i) that the normal NO stretching band, ν_2, is split into two strong bands at 894 and 929 cm.$^{-1}$, comparable with the values 886 cm.$^{-1}$ found in the infrared spectrum [3] of



(I) (II) (III)

the vapour (presumably non-H-bonded) and 925 cm.$^{-1}$ in the Raman [7] and infrared [8] spectra of the liquid (presumably H-bonded), and (ii) that there are two main bands and a subsidiary band in the OH stretching region (3200—3600 cm.$^{-1}$).

Structure (I), proposed by Chédin [5] for the hemihydrate in concentrated nitric acid solution, does not satisfy the first feature of the spectrum because both N–OH groups would be expected to be equivalent to each other. Accordingly we suggest structure (II) for the $(HNO_3)_2,H_2O$ species under the present conditions, and recognise that there may be some contribution from an ionic structure (III) to account for the 1401 cm.$^{-1}$ (possibly nitrate) band in the spectrum. At high concentrations of nitric acid in the organic phase the non-hydrogen-bonded N–OH group may be expected to form larger aggregates with other monomers or dimers and thus to cause deviations from the proposed equation at C_a >14M.

Experimental.—The initial aqueous nitric acid concentration, C_i, was determined by titrating an aliquot part with standard alkali against Methyl Orange. Equal volumes of the nitric acid (diluted " AnalaR " grade) and toluene (sulphur-free " AnalaR " grade) were stirred together for 2 or 10 min. at 20°, the phases were separated by centrifugation, and an aliquot part of the organic phase was titrated electrometrically with standard alkali. The equilibrium aqueous nitric acid concentration, C_a, was calculated by difference for initial concentrations of less than 14M-nitric acid. Toluene slowly became coloured in contact with 16M-nitric acid, and titrations showed a gradual loss of acid amounting to 0·1M after 2 min. and ~1M after 10 min. No loss of acid, even at 16M, occurred with " AnalaR " benzene, n-dodecane, odourless kerosene, cyclohexane (Spectrosol), and " AnalaR " carbon tetrachloride. Water in the toluene phase was determined by the Karl Fischer method.

Infrared spectra of nitric acid extracted from aqueous 14M-nitric acid into benzene, carbon tetrachloride, and n-dodecane were measured from 2 to 15 microns (on liquid films between silver chloride plates separated by an ~10 μ Polythene spacer) on a Hilger H.800 double-beam spectrometer with a rock-salt prism. Silver chloride plates have been shown [8] to be satisfactory for use with concentrated nitric acid solutions.

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[*Received, July 8th*, 1960.]

[4] Erdmann, *Z. anorg. Chem.*, 1902, **32**, 431.
[5] Chédin, *J. Chim. phys.*, 1952, **49**, 109.
[6] Gillespie, Hughes, and Ingold, *J.*, 1950, 2552.
[7] Ingold and Millen, *J.*, 1950, 2612.
[8] Marcus and Fresco, *J. Chem. Phys.*, 1957, **27**, 564.

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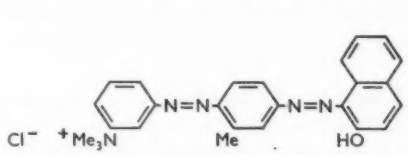
19. *Studies in Adsorption. Part XIII.* Anomalous (Endothermic) Effects of Adsorption on Inorganic Solids.*

By C. H. Giles, J. J. Greczek, and S. N. Nakhwa.

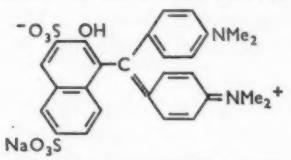
The adsorption of two dyes from water on to inorganic surfaces is found to be apparently endothermic, saturation adsorption rising with temperature. Both dyes are associated in aqueous solution. From a dissociating solvent (methanol) the adsorption is normal, the amount sorbed falling with rise in temperature. The anomalous adsorption from water is considered to be the result of partial dissociation at the substrate surface.

Adsorption of dye as micelles appears to occur even from methanol, and it is suggested that association takes place at the moment of adsorption.

Adsorption from solution is usually, like vapour-phase adsorption, exothermic, so that a rise in temperature causes a decrease in saturation adsorption. In a few cases change in temperature produces no change in adsorption, but so far all such cases are apparently



Janus Red B (C.I. 26,115)



Lissamine Green BN (C.I. 44,090)

ion-exchange adsorption, usually on organic surfaces.[1] Little is known of systems showing a reversed temperature effect, *i.e.*, where rise in temperature increases the saturation

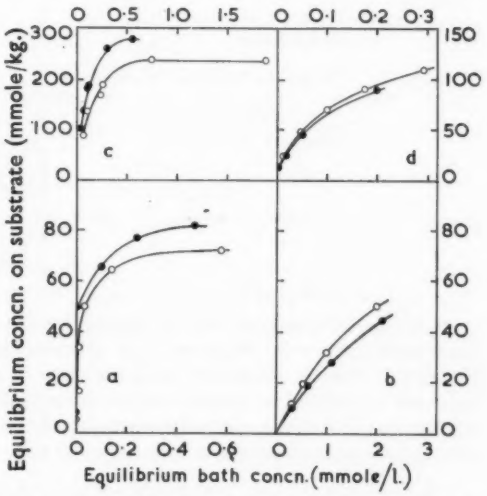


Fig. 1. *Solution adsorption isotherms.*

(a) *Janus Red B* (C.I. 26,115) *on silica (specific surface area* 0·108 × 10^5 cm.²/g.) *from water, at* (○) 30°, (●) 50°.

(b) *As* (a), *from methanol, at* (○) 16°, (●) 37° (*silica, specific surface area* 0·062 × 10^5 cm.²/g.).

(c) *Lissamine Green BN* (C.I. 44,090) *on chromatographic alumina* (ref. 1*b*; *specific surface area* 5 × 10^5 cm.²/g.) *at* (○) 20°, (●) 42°.

(d) *As* (c), *from methanol, at* (○) 19·5°, (●) 36·5°.

Apparent heats of adsorption, calc. from the curves, are: (a) +5·8 ± 1·4; (b) −2·4 ± 0·5; (c) +6·0 ± 2·6; (d) −1·7 ± 0·6 kcal./mole.

adsorption: previously recorded cases include the adsorption of (i) two azo-dyes (C.I. 14,600, anionic; C.I. 26,115, cationic) from water by silica; (ii) butanol from its mixtures

* Part XII, *J.*, 1961, 58.

[1] See, *e.g.*, (*a*) Allingham, Cullen, Giles, Jain, and Woods, *J. Appl. Chem.*, 1958, **8**, 108; (*b*) Cummings, Garven, Giles, Rahman, Sneddon, and Stewart, *J.*, 1959, 535; (*c*) Giles, Mehta, Rahman, and Stewart, *J. Appl. Chem.*, 1959, **9**, 457 [Fig. 5 (left), for *f*, *g* read *g*, *f*; Fig. 6, C_F scale for (XIV) is 0—50 units].

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with water by charcoal;[2] (iii) succinic acid from water or ethanol, by charcoal;[3] and (iv) long-chain sulphate esters by wool.[4] Bikerman[3] attributes this behaviour to a negative temperature coefficient of the solubility of the solute or to a steep simultaneous decrease of the real adsorption of the solvent.

Cause of the Anomaly.—In the present work we have examined the adsorption of several dyes by inorganic solids. Some results are shown in Fig. 1. In the two cases in which adsorption rises with temperature there is good evidence that the dyes are highly aggregated in solution; thus the solutions do not obey Beer's law and show marked light-scatter. Further, when a dissociating solvent is used (methanol) the adsorption is normal, falling with rise in temperature. The apparent endothermic nature of these systems is therefore a result of the aggregation of the solutes in solution, as shown in the energy-level diagrams (Fig. 2). In these cases it appears that the solute is partly dissociated on adsorption.

Nature of Association on Substrate.—Two facts indicate that the adsorbed layer of both dyes (even in methanol) consists of aggregated particles, and is not a true unimolecular layer: (*a*) the shape of the isotherms (*L*2, ref. 5),* and (*b*) the high " coverage factor " (*i.e.*, the amount of dye adsorbed to fill a " monolayer " divided by the amount calculated for a unimolecular layer) which is *ca.* 30 for the red dye at 16° and *ca.* 2 for the green dye at 19·5°.

FIG. 2 (*a*). *Energy-level diagram for normal (exothermic) adsorption of dye on solid surface.*

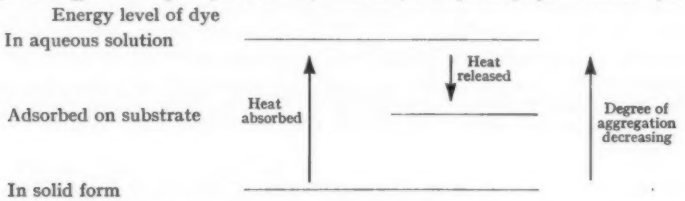
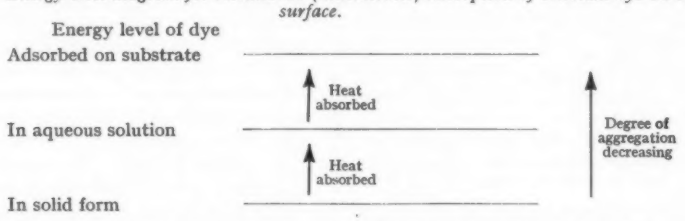


FIG. 2 (*b*). *Energy-level diagram for anomalous (endothermic) adsorption of colloidal dye on solid surface.*



It is especially interesting that aggregates can apparently be adsorbed under conditions (high temperature in disaggregating solvents) in which the dyes must be molecularly dispersed. This is consistent with the view already expressed that aromatic solutes in water are associated at a solid surface during adsorption, either immediately before or at the moment of attachment to the surface. Even highly sulphonated dyes, the most likely to be molecularly dispersed in water, appear to behave thus.[6,7]

* In a unimolecular layer, both dyes would be oriented end-on to the surface and so would be expected to give the *S* isotherm (for reasons see ref. 5).

[2] Bartell, Thomas, and Fu, *J. Phys. Chem.*, 1951, **55**, 1456.

[3] Bikerman, " Surface Chemistry, Theory and Applications," Academic Press Inc., New York, 2nd edn., 1958, p. 294; cf. Heyne and Polanyi, *Z. phys. Chem.*, 1928, **132**, 284.

[4] Aickin, *J. Soc. Dyers Colourists*, 1944, **60**, 60.

[5] Giles, MacEwan, Nakhwa, and Smith, *J.*, 1960, 3973.

[6] Baxter, Giles, and Rahman, *Textile Res. J*, in the press.

[7] (*a*) Campbell and Giles, *J. Soc. Dyers and Colourists*, 1958, **74**, 164; (*b*) Campbell, Cathcart, Giles, and Rahman, *Trans. Faraday Soc.*, 1959, **55**, 1631.

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Orange I.—This dye also gives anomalous isotherms on silica,[1a] but adsorption from aqueous pyridine or methanol is also anomalous. These unexpected results were found to be due to slow decolorisation of the dye solutions at high temperature, presumably owing to hydrolysis of the azo-group. The red and the green dye were not decolorised in this way.

Experimental.—The methods have been described.[1] The dyes were commercial products recrystallised three times from 1 : 1 v/v ethanol–water, which gave constant molar extinctions. The state of aggregation of the dyes in solution was detected qualitatively by nephelometric measurement (EEL instrument). Molecularly dispersed solutions, in *e.g.*, methanol or pyridine, gave zero readings.

The authors thank Professor P. D. Ritchie for his interest, T. Burniston and F. D. Hart for help with experimental work, and the Ministry of Education for a scholarship (to J. J. G.).

DEPARTMENT OF CHEMICAL TECHNOLOGY, THE ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY, GLASGOW, C.1. [*Received, June 17th,* 1960.]

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20. *The Ammonolysis of Hexahalogenotitanates.*

By G. W. A. FOWLES and D. NICHOLLS.

The ammonolysis of several hexachlorotitanates (M_2TiCl_6, where M = NH_4, NH_3Me, K) and diammonium hexabromotitanate has been studied; in each case two titanium–halogen bonds are ammonolysed. The thermal decomposition of the products has been examined.

HALIDES of most of the transition metals in their highest valency state are ammonolysed in liquid ammonia,[1,2] and the ammonobasic metal halides formed can often be isolated because they are insoluble in liquid ammonia. This insolubility is probably due to the highly polymeric nature of the compounds. They dissolve, however, in highly concentrated solutions of ammonium halides, and in view of recent ion-exchange experiments with solutions of titanium(IV) iodide in liquid ammonia,[2] and by analogy with acids $H_2[Ti(OH)_nCl_{6-n}]$ formed in aqueous systems,[3] it seems likely that the solution is brought about through the formation of ammono-acids, *e.g.*:

$$TiX(NH_2)_3 + NH_4X \text{ (excess)} \longrightarrow (NH_4)_2[TiX_3(NH_2)_3]$$

To obtain further support for this idea, we have examined the ammonolysis of several hexahalogenotitanates.

The hexachlorotitanates dissolve almost completely, and the hexabromotitanate completely, in ammonia; ammonolysis undoubtedly occurs, giving a soluble complex, and information on the extent of this ammonolysis is provided by tensimetric experiments (cf. Table 1 and Figs. 1a, 2a, and 3a). This tensimetric procedure can give only an average value for the number of metal–chlorine bonds ammonolysed when the product is insoluble in ammonia, and hence polymeric, but gives a truer picture for the hexahalogenotitanates where the products are largely soluble. Considering the ammonolysis of the diammonium hexachloro- and hexabromo-titanates, we observe that four mols. of ammonium halide are present. There are two possible explanations, namely:

$$\text{(i)}\ (NH_4)_2TiX_6 \longrightarrow (NH_4)_2[TiX_2(NH_2)_4] + 4NH_4X$$

$$\text{(ii)}\ (NH_4)_2TiX_6 \longrightarrow (NH_4)_2[TiX_4(NH_2)_2] + 2NH_4X$$

$$\downarrow$$

$$TiX_2(NH_2)_2 + 4NH_4X$$

[1] Fowles and Nicholls, *J.*, 1958, 1687.
[2] Fowles and Nicholls, *J.*, 1959, 990.
[3] Rumpf, *Ann. Chim.* (*France*), 1937, **8**, 456.

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TABLE 1.

Halide	Solubility (%) with excess of ammonia	Insoluble product, washed with ammonia	Mol. ratio NH_4X/Ti detected tensimetrically
$TiCl_4$	5	$TiCl(NH_2)_3$	2·7
$(NH_4)_2TiCl_6$	90	$TiCl(NH_2)_3 + TiCl_2(NH_2)_2$	4·0
K_2TiCl_6	70	,, ,,	2·0
$(NH_3Me)_2TiCl_6$	90	,, ,,	—
$TiBr_4$	70	$TiBr(NH_2)_3 + TiBr_2(NH_2)_2$	2·7
$(NH_4)_2TiBr_6$	100	—	4·0
TiI_4	100	—	2·5

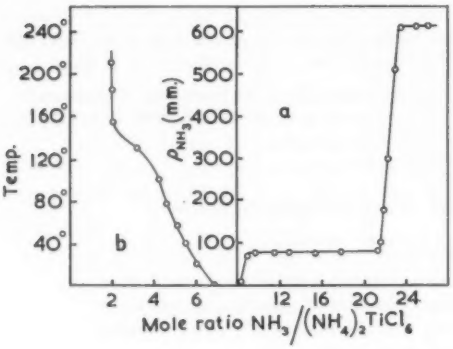
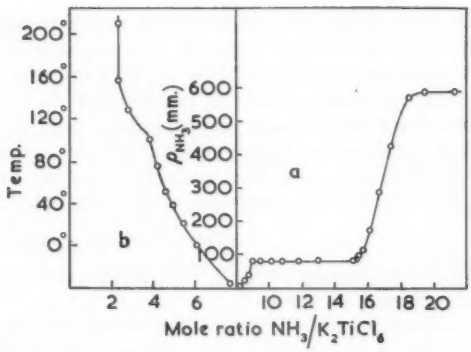


FIG. 1. *The* NH_3–$(NH_4)_2TiCl_6$ *system.*
(a) *Tensimetric plot.*
(b) *Thermal decomposition.*

FIG. 2. *The* NH_3–K_2TiCl_6 *system.*
(a) *Tensimetric plot.*
(b) *Thermal decomposition.*



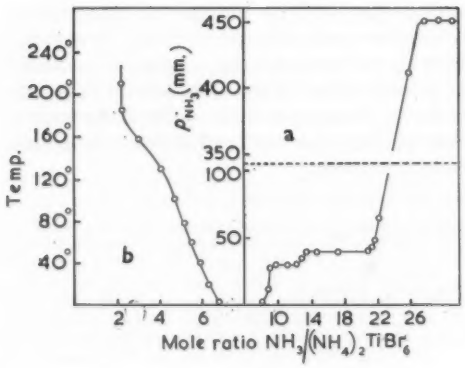


FIG. 3. *The* NH_3–$(NH_4)_2TiBr_6$ *system.*
(a) *Tensimetric plot.*
(b) *Thermal decomposition.*

In scheme (i), four mols. of ammonium halide are produced, the complex is stable under the conditions of the tensimetric runs, and the four mols. of ammonium halide form the appropriate ammoniates. In scheme (ii), only two titanium–halogen bonds are ammonolysed, but breakdown of the complex (in the absence of excess of ammonia) leads to the formation of four mols. of ammonium halide.

The complex is unlikely to remain intact under the tensimetric conditions, because it certainly does not in the analogous reactions of titanium(IV) bromide and iodide with ammonia, where although the solutions contain complex anions, virtually all the ammonium halide is detected tensimetrically. Under scheme (ii) we get a consistent explanation whereby a soluble complex is formed with excess of ammonia; when the ammonia is removed the complex breaks down into the ammonobasic titanium(IV) halide and ammonium halide. Hence under the tensimetric conditions we should expect to find four mols. and two mols. of ammonium halide produced by the ammonolysis of the diammonium and dipotassium salts respectively.

Although two titanium–chlorine bonds are ammonolysed in both hexachlorotitanates, a further reaction will occur with the potassium salt because potassium chloride has only a moderate solubility in liquid ammonia and will be precipitated:

$$K_2TiCl_6 \xrightarrow{NH_3} K_2[TiCl_4(NH_2)_2] + 2NH_4Cl$$
$$\longrightarrow (NH_4)_2[TiCl_4(NH_2)_2] + 2KCl$$

This removal of ammonium chloride is unlikely to result in further ammonolysis of the complex ion because the acidity of the solution (*i.e.*, concentration of NH_4^+) is unchanged.

The small residue remaining on filtration of the solution formed by diammonium hexachlorotitanate had a composition corresponding to a mixture of $TiCl_2(NH_2)_2,2NH_3$ and $TiCl(NH_2)_3$; this is presumably a polymer of variable composition, in which the Ti : Cl ratio can be lowered close to 1 : 1 by prolonged washing with ammonia. A similar residue is obtained from the dipotassium salt, except that it is somewhat contaminated with potassium chloride.

The reaction of bismethylammonium hexachlorotitanate with ammonia is essentially the same as that of the other hexachloro-salts, except that there is also interaction between ammonia and the methylammonium ion:

$$(NH_3Me)X + NH_3Me \longrightarrow (NH_4)X + NH_3Me$$

This reaction goes almost to completion in the presence of excess of ammonia. Direct evidence for this displacement comes from the work of Aida [4] who from Raman spectra measurements showed free methylamine to be present in solutions of methylamine hydrochloride in liquid ammonia. A similar displacement of one amine from amine hydrochloride and bisalkylammonium hexachlorozirconates by another amine has been reported recently.[5]

Removal of excess of ammonia at −36° from products formed in the tensimetric experiments leaves ammonolytic mixtures with the overall compositions of octaammoniates:

$$(NH_4)_2TiX_6,8NH_3 \equiv TiX_2(NH_2)_2,4NH_3 + 4NH_4X,$$
$$K_2TiCl_6,8NH_3 \equiv TiCl_2(NH_2)_2,4NH_3 + 2NH_4Cl + 2KCl$$

When the mixtures are heated *in vacuo* ammonia is lost and examination of the thermal decomposition curves (Figs. 1b, 2b, and 3b) suggests a modest stability for mixtures with the overall composition $M_2TiX_6,4NH_3$.

The decomposition above 130° is in every case of a more fundamental nature. Thus

[4] Aida, *Sci. Reports Res. Inst. Tohôku Univ.*, 1956, Ser. A, **8**, 441.
[5] Drake and Fowles, *J. Inorg. Nuclear Chem.*, in the press.

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the products from the diammonium hexabromotitanate(IV)–ammonia reaction decompose between 130° and 210° to produce a red sublimate of the simple adduct $TiBr_4,2NH_3$ (this has been previously obtained from the titanium(IV) bromide–ammonia system under similar conditions), and ammonium bromide also sublimes, leaving finally a residue of composition approaching TiNBr. It seems that the ammonobasic titanium(IV) bromide, $TiBr_2(NH_2)_2$, may either decompose [cf. reactions (*a*) and (*b*)] or interact with ammonium bromide [cf. reactions (*c*) and (*d*)], both probably occurring simultaneously:

$$\left.\begin{array}{l}(a)\ TiBr_2(NH_2)_2 \longrightarrow TiBr_2(NH) + NH_3 \\ (b)\ TiBr_2(NH) \longrightarrow TiNBr + HBr\end{array}\right\} \longrightarrow NH_4Br$$

$$(c)\ TiBr_2(NH_2)_2 + NH_4Br \longrightarrow TiBr_2(NH_2) + 2NH_3$$

$$(d)\ TiBr_2(NH_2) + NH_4Br \longrightarrow TiBr_4 + 2NH_3 \longrightarrow TiBr_4,2NH_3$$

The diammoniate of titanium(IV) bromide is formed on the cooler part of the wall of the reaction vessel through recombination of ammonia and the bromide; some ammonium bromide is formed by a similar process, and some sublimes directly from the reaction mixture.

Both hexachlorotitanate–ammonia products decompose analogously, although the residue from the dipotassium salt contains the involatile potassium chloride. The yellow sublimate is probably the diammoniate $TiCl_4,2NH_3$, since this has previously been reported by Antler and Laubengayer [6] to be a product of the gas-phase reaction of titanium(IV) chloride and ammonia.

The transient blue colour formed by solutions of some of the residues on hydrolysis in dilute sulphuric acid indicates that there is a little reduction of titanium to the tervalent state; this is not perhaps surprising in view of the reducing conditions.

Experimental

Materials.—The preparation of the hexahalogenotitanates is described elsewhere.[7] Liquid ammonia was dried over sodium.

Analysis.—Gravimetric methods were used to determine titanium (as dioxide), chlorine (as silver chloride), and bromine (as silver bromide). Potassium was determined by difference. Nitrogen was determined as ammonia. Unless otherwise stated, all products were hydrolysed with dilute sulphuric acid before analysis, and colourless solutions were formed.

Reactions and Tensimetric Studies.—Since all reactants and products were readily hydrolysed, studies were made under rigorously anhydrous conditions in the usual type of all-glass closed-vacuum system.[8]

(a) *Solubility studies in liquid ammonia.* (i) Diammonium hexachlorotitanate dissolved almost completely in excess of liquid ammonia to give a yellow solution. A little yellow solid remained on filtration, and this was washed several times, kept *in vacuo* for several hours at room temperature, and then analysed (Found: Ti : Cl : N = 1·00 : 1·65 : 3·58). A mixture of yellow and white solids was obtained by evaporation of the filtrate, and this was hydrolysed *in situ* and analysed. Table 2 shows the analytical results expressed in the form of N : Cl ratios; the soluble portion is assumed to be a mixture of some ammonobasic titanium(IV) chloride with ammonium chloride, and the N : Cl ratio is obtained from the nitrogen and chlorine still unaccounted for after allowing for that associated with the titanium. This ratio should be 1 : 1 (*i.e.*, NH_4Cl).

Table 2. *Analysis of the soluble portion.*

Run no.	$Ti(NH_2)_4$	$TiCl(NH_2)_3$	N : Cl ratio if Ti present as $TiCl_2(NH_2)_2,2NH_3$	$TiCl_3(NH_2),2NH_3$
1	1·00 : 0·67	1·00 : 0·97	1·00 : 0·96	1·00 : 1·52
2	1·00 : 0·73	1·00 : 1·03	1·00 : 1·04	1·00 : 1·58

[6] Antler and Laubengayer, *J. Amer. Chem. Soc.*, 1955, **77**, 5250.
[7] Fowles and Nicholls, *J. Inorg. Nuclear Chem.*, in the press.
[8] Fowles and Pollard, *J.*, 1953, 2588.

(ii) *Triaminochloridotitanium*(IV), prepared by Fowles and Pollard's method [8] [Found: Ti, 35·7; N, 32·2. $TiCl(NH_2)_3$ requires Ti, 36·4; N, 32·0%], partly dissolved in a solution of ammonium chloride in ammonia, the solubility increasing with the concentration of ammonium chloride. The solubility was far less than that of $VCl(NH_2)_3$ (in NH_4Cl–NH_3), and appreciably less than that of $TiBr(NH_2)_3$ (in NH_4Br–NH_3).

(iii) Dipotassium hexachlorotitanate largely dissolved to a yellow solution. The residue left on filtration continued to dissolve when washed with ammonia, but the filtrate became colourless after three washings, although it still deposited a white solid on evaporation. The residue of 15 washings with 50 ml. of ammonia was analysed after it had been heated *in vacuo* at 40° for some hours (Found: Ti, 28·6; Cl, 23·6; NH_2, 40·0; K, 7·8%; corresponding to Ti : Cl : N : K = 1·00 : 1·89 : 2·46 : 0·33, or 0·33KCl + Ti : Cl : N = 1·00 : 1·56 : 2·46). The soluble product contained almost all the original potassium (Found: Ti, 9·78; Cl, 46·6; NH_3, 14·1; K, 29·5%; corresponding to Ti : Cl : N : K = 1·00 : 6·44 : 3·84 : 3·70, or 3·70KCl + Ti : Cl : N = 1·00 : 2·74 : 3·84).

(iv) Bismethylammonium hexachlorotitanate resembled the potassium salt in its solubility. Twelve washings left an orange-yellow residue (0·16 g.) (Found: Ti, 26·3; Cl, 33·0; N, 32·6%; corresponding to Ti : Cl : N = 1·00 : 1·69 : 4·24). As excess of ammonia was removed from the filtrate, the last drops smelled strongly of methylamine; the orange-pink residue (0·854 g.) was analysed (Found: Ti, 10·3; Cl, 51·5; N, 29·2%; corresponding to Ti : Cl : N = 1·00 : 6·74 : 9·66). On the assumption that the difference in the total from 100% is due to either H (from ammonia), or H and CH_3 (from methylamine), it can be calculated that more than 90% of the original methylamine had been expelled by ammonia.

(v) Diammonium hexabromotitanate was entirely soluble in excess of ammonia, giving a yellow solution; the pale yellow heterogeneous solid obtained from the filtrate was analysed (Found: Ti, 7·09; Br, 69·6; NH_3, 21·1%; corresponding to Ti : Br : N = 1·00 : 5·88 : 8·38).

(b) *Tensimetric studies.* These were carried out at −36°, and the product thermally decomposed in the usual way.[8] Results obtained for the systems of ammonia with diammonium and dipotassium hexachlorotitanates, and diammonium hexabromotitanate, are illustrated in Figs. 1, 2, and 3 respectively. In view of the liberation of methylamine from the ammonia–bismethylammonium hexachlorotitanate reaction, this system was not examined tensimetrically.

With both of the hexachlorotitanates, the products changed from pale yellow at −36° (overall composition $M_2TiCl_6,8NH_3$) to orange at 100° (overall composition $M_2TiCl_6,4NH_3$). When the products were heated above 130° a yellow sublimate started to be formed, and above 160° a substantial white sublimate was formed in addition. The compositions given in Figs. 1b, 2b, and 3b include any sublimed material. The residue from the diammonium salt reaction, which was red-brown after being heated to 210°, had an analysis corresponding to Ti : Cl : N = 1·00 : 1·52 : 1·01. The residue from the dipotassium salt reaction became black when heated above 200°; samples were taken for analysis from reaction products heated to 210° and 360° [Found (for the 210° product): Ti, 17·1; Cl, 47·0; N, 3·36; K, 32·5%; corresponding to 2·34KCl + Ti : Cl : N = 1·00 : 1·38 : 0·67. Found (for the 360° product): Ti, 15·5; Cl, 46·8; N, 2·94; K, 34·8%; corresponding to 2·75KCl + Ti : Cl : N = 1·00 : 1·33 : 0·65]. These residues, which contained all the potassium originally introduced as K_2TiCl_6, dissolved in dilute sulphuric acid to give pale-blue solutions which rapidly became colourless.

In the thermal decomposition of the products from the NH_3–$(NH_4)_2TiBr_6$ reaction, a bright red sublimate appeared at 155°, and a copious white sublimate formed at 180° [Found, for mixed sublimate (0·47 g.): Ti, 6·27; Br, 81·4; N, 10·5%; corresponding to Ti : Br : N = 1·00 : 7·78 : 5·73 (approximately $TiBr_4,2NH_3$ + 3·73NH_4Br]. The black residue (0·039 g.) remaining at 210° dissolved in dilute sulphuric acid with the formation of a rapidly fading blue colour (Found: Ti, 29·8; Br, 61·7; N, 8·9%; corresponding to Ti : Br : N = 1·00 : 1·24 : 1·02).

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21. *Physicochemical Studies of Some Cyclic Carbonates. Part III.*[1] *Electrical Conductivities in Ethylene Carbonate.*

By R. F. Kempa and W. H. Lee.

Conductometric measurements in ethylene carbonate of a number of 1 : 1-electrolytes indicate that complete ionisation occurs in this solvent. Positive departures of some of the Kohlrausch plots from the theoretical Onsager lines are explained in terms of extensive solvation of the smaller cations; negative deviations from the Onsager slopes are attributed to a small degree of ion-pair formation. A method is suggested for the estimation of apparent ionic radii and hence of approximate solvation numbers from conductance data. The values of the solvation numbers obtained by this method for the alkali-metal ions in ethylene carbonate support the increase of ionic conductance along the series: $Li^+ < Na^+ < K^+ < Rb^+ < Cs^+$.

It was reported in Part I of this series that ethylene carbonate is a highly polar solvent, having a dipole moment $\mu = 4{\cdot}87$ D, and dielectric constant $\varepsilon = 89{\cdot}6$, at 40°. Subsequently, the Harris–Alder correlation parameter [2] g was calculated from these data. The value $g = 1{\cdot}25$ for ethylene carbonate at 40° suggests that the liquid is only slightly associated, in contrast to substances of similar and higher dielectric constant, *e.g.*, water and the *N*-monomethyl-amides, all of which are strongly hydrogen-bonded in the condensed phase. It was felt, therefore, that conductometric measurements of electrolyte solutions in ethylene carbonate would provide useful information about the electrochemical behaviour of electrolytes in solvents of high dielectric constant, which, however, in contrast to water and similar hydrogen-bonded solvents, are not appreciably associated.

The alkali-metal halides are, in general, too insoluble in ethylene carbonate for conductivity studies to be made; however, we found the alkali-metal perchlorates and the tetra-alkylammonium halides to be sufficiently soluble for this purpose. The electrical conductances of such 1 : 1-electrolytes in ethylene carbonate have accordingly been measured at 40°.

Experimental

Electrical conductances were measured in borosilicate-glass conductivity cells having rigid bright platinum electrodes; the cell constants were approximately 0·1 cm.$^{-1}$, as determined from conductance measurements of potassium chloride solutions of known concentration, using the equation: [3]

$$\Lambda_c(KCl) = 149{\cdot}92 - 93{\cdot}85\sqrt{c} + 50c \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Although the values of the constants in this equation refer to conductivities at 25°, the cell constants were assumed to be applicable at 40°; no reference solutions are available for determining cell constants at this temperature.

Measurements were made by means of a conventional Wheatstone bridge circuit, energised by an oscillator of 1500 c./sec. frequency, the off-balance voltage being amplified, detected, and observed on a microammeter.

Solvent.—Ethylene carbonate was purified as described in Part I, and had the following physical properties at the temperature of the experiments: Density $d_4^{40} = 1{\cdot}3208$ g. cm.$^{-3}$, viscosity $\eta = 1{\cdot}850 \times 10^{-2}$ ps., specific conductivity $\kappa = 0{\cdot}04 - 0{\cdot}09 \times 10^{-6}$ ohm^{-1} cm.$^{-1}$; a solvent correction was determined and applied for each solution measured.

Solutes.—Lithium perchlorate was prepared by heating "AnalaR" lithium nitrate with perchloric acid, and recrystallising the salt twice from water. It was dried to constant weight by heating it to 300° in a current of dried air.

Sodium perchlorate was prepared by dissolving sodium carbonate in perchloric acid,

[1] Part II, Kempa and Lee, *J.*, 1959, 1576.
[2] Harris and Alder, *J. Chem. Phys.*, 1953, **21**, 1031.
[3] Shedlovsky, *J. Amer. Chem. Soc.*, 1932, **54**, 1411.

recrystallising the anhydrous salt from water at a temperature above 50°, and drying it to constant weight in an air-bath at about 250°.

Potassium perchlorate was obtained by twice recrystallising a commercial sample from water and drying it in an evacuated desiccator (P_2O_5).

Rubidium and cæsium perchlorates were prepared by dissolving the carbonates in perchloric acid, recrystallising the precipitates from water, and drying.

Tetramethylammonium iodide was prepared from a commercial sample by partial crystallisation from ethyl acetate.

Tetraethylammonium iodide was purified by twice recrystallising a commercial sample of the salt from ethyl acetate containing about 5% of ethanol.

Tetraethylammonium bromide was prepared by treating triethylamine with ethyl bromide in alcoholic solution at 70°. The salt was recrystallised from ethyl acetate.

Tetraethylammonium perchlorate was obtained from the iodide by precipitation with dilute perchloric acid in aqueous alcohol. The salt was washed with cold water and dried *in vacuo* (P_2O_5).

Tetra-n-butylammonium iodide was purified by twice recrystallising a commercial sample from ethyl acetate.

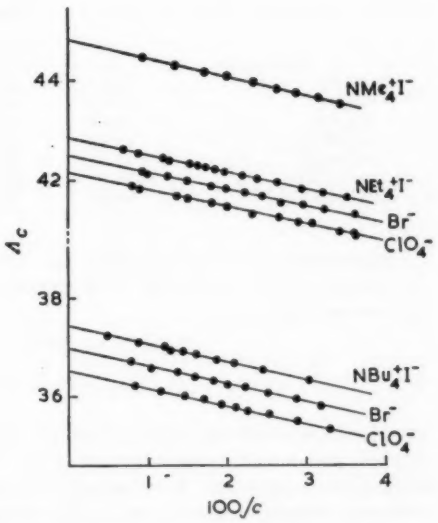

FIG. 1. *Equivalent conductances* Λ_c *(cm.*^{2} *ohm*$^{-1}$ *g.-equiv.*$^{-1}$*) of some tetra-alkylammonium salts in ethylene carbonate at* 40°.

Tetra-n-butylammonium bromide was prepared by heating n-butyl bromide with tri-n-butylamine in a sealed tube at 100° for 48 hr. The salt was recrystallised several times from ether–ethyl acetate.

Tetra-n-butylammonium perchlorate was prepared from the iodide by metathesis with silver perchlorate. The crude material was recrystallised from ethyl acetate.

Solutions for conductivity measurement were prepared by addition of weighed amounts of stock solution to a known weight of solvent in the cell; a current of dry nitrogen was passed over the solution during the addition.

(1) *Conductivity of some tetra-alkylammonium salts in ethylene carbonate.*

Results.—The Λ_c–$\sqrt{c}$ plots for the tetramethyl-, tetraethyl- and tetra-n-butyl-ammonium iodides, and for the tetraethyl- and tetra-n-butyl-ammonium bromides and perchlorates are shown in Fig. 1. The results for one of these electrolytes, typical of all, are given in Table 1.

The extrapolated Λ_0 values were substituted in the Debye–Huckel-Onsager equation:

$$\Lambda_c = \Lambda_0 - \left[\frac{82{\cdot}5}{(\varepsilon T)^{\frac{1}{2}}\eta} + \frac{8{\cdot}20 \times 10^5}{(\varepsilon T)^{\frac{3}{2}}}\Lambda_0\right]\sqrt{c} \quad . \quad . \quad . \quad . \quad . \quad (2)$$

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TABLE 1. *Conductivity of tetraethylammonium perchlorate in ethylene carbonate at* 40°.

10^4c (mole l.$^{-1}$)	$10^2\sqrt{c}$	Λ_c (cm.^{2} ohm^{-1} g.-equiv.$^{-1}$)	10^4c (mole l.$^{-1}$)	$10^2\sqrt{c}$	Λ_c (cm.^{2} ohm^{-1} g.equiv.$^{-1}$)	10^4c (mole l.$^{-1}$)	$10^2\sqrt{c}$	Λ_c (cm.^{2} ohm^{-1} g.-equiv.$^{-1}$)
0·6296	0·7934	41·85	3·8141	1·9530	41·45	9·6879	3·1117	41·07
0·7779	0·8820	41·83	5·5254	2·3506	41·32	12·0112	3·4657	40·94
1·8959	1·3769	41·65	7·5975	2·6945	41·21	13·5040	3·6749	40·86
2·3054	1·5184	41·60	8·6332	2·9382	41·12	13·6641	3·6965	40·85
3·2954	1·8152	41·50						

and the theoretical limiting slopes determined. In this equation, Λ_c is the equivalent conductance at concentration c (g.-equiv. l.$^{-1}$), Λ_0 the extrapolated equivalent conductance at infinite dilution, ε the dielectric constant, and η the viscosity, of the solvent at $T°$ K.

The Λ_0 values and the theoretical limiting slopes are recorded in Table 2, together with the experimental Λ_c–$\sqrt{c}$ slopes and their deviations from the theoretical, and the values of the Walden product $\Lambda_0\eta$ for each solute.

TABLE 2.

Electrolyte	Λ_0	Slope (exptl.)	Slope (theor.)	$\frac{100\Delta \text{ Slope}}{\text{Theor. slope}}$	$\Lambda_0\eta$
Me_4NI	44·81	37·0	34·44	+7·5	0·828
Et_4NI	42·83	35·0	34·09	+2·6	0·792
Et_4NBr	42·48	34·8	34·03	+2·4	0·785
Et_4NClO_4	42·13	34·4	33·91	+1·2	0·779
n-Bu_4NI	37·41	35·2	33·15	+6·0	0·692
n-Bu_4NBr	36·97	36·3	33·07	+9·7	0·683
n-Bu_4NClO_4	36·52	35·9	32·99	+8·8	0·975

Discussion.—The Λ_c–$\sqrt{c}$ plots are linear within the concentration range studied. The slopes deviate positively from equation (2) in the appropriate form for this solvent and temperature:

$$\Lambda_c = \Lambda_0 - (26{\cdot}61 + 0{\cdot}175\Lambda_0)\sqrt{c} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$= \Lambda_0 - S\sqrt{c}, \text{ where } S = 26{\cdot}61 + 0{\cdot}175\Lambda_0$$

The deviations depend mainly upon the cation, and are large and positive for the tetramethyl- and tetrabutyl-ammonium salts; such deviations are usually regarded as due to incomplete dissociation, or to ion-pair formation. The linearity of the experimental slopes indicates complete dissociation of the electrolytes at these concentrations, and seems to be best described by the second of six characteristic patterns listed by Fuoss and Accascina.[4] This behaviour is ascribed to ion-pair formation with the point of inflection of the curve lying below the minimum concentration studied.

In a medium of dielectric constant 89·6, at very low concentration, association of the solute ions is unlikely to extend beyond pair-formation. We can calculate a dissociation constant for the ion-pairs as follows. If their degree of dissociation at molarity c is α, we may write from equation (3)

$$\Lambda_c = \alpha[\Lambda_0 - S.\sqrt{(c\alpha)}] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The iteration process of solving equation (4) for α by successive approximations, starting from $\alpha_0 = \Lambda_c/\Lambda_0$, has been considered by Fuoss;[5] he tabulates a function F of the derived variable $Z = (S/\Lambda_0^{\frac{3}{2}})\sqrt{(c\Lambda_c)}$, such that the final value of α in equation (4) is given by Λ_c/Λ_0F. It will be observed that F is a function of the molarity of the solution. From the law of mass action, if K is the thermodynamic dissociation constant for the ion-pairs,

[4] Fuoss and Accascina, "Electrolytic Conductance," Interscience, New York, 1959, p. 266.
[5] Fuoss, *J. Amer. Chem. Soc.*, 1935, **57**, 488.

$K = c\alpha^2 f_\pm^2/(1 - \alpha)$. To solve this equation for K, $f_\pm$ the mean-ion activity coefficient of the solute at each concentration is required. This can be calculated from the equation [6]

$$-\log f_\pm^2 = \frac{3{\cdot}6494 \times 10^6}{(\varepsilon T)^3} \cdot \frac{\sqrt{c}}{1 + \beta a}$$

where

$$\beta = 5{\cdot}0293 \times 10^9 \sqrt{c}/(\varepsilon T)^{\frac{1}{2}} \quad \ldots \quad (5)$$

and a is the distance of closest approach of the ions. However, as equation (3) is the limiting form of the law, it seems more consistent to calculate $f_\pm$, for the evaluation of K, by the limiting form of equation (5), *i.e.*, by the omission of the term $(1 + \beta a)$. We thus obtain, for the ion-pair dissociation constant of tetrabutylammonium bromide in ethylene carbonate, the mean value $K_{40°} = 0{\cdot}26 \pm 0{\cdot}04$, and for tetramethylammonium iodide, $K_{40°} = 0{\cdot}33 \pm 0{\cdot}08$. These solutes appear to be associated, in the form of ion-pairs, to about the same extent as thallous chloride in aqueous solution,[7] for which the dissociation constant has the value $K_{25°} = 0{\cdot}32 \pm 0{\cdot}03$.

Kohlrausch's law of independent ionic mobilities applies to these solutes in ethylene carbonate solution, as the following results show:

	Br^-	I^-	ClO_4^-
$\lambda°_{Et_4N^+} - \lambda°_{n\text{-}Bu_4N^+}$	5·51	5·42	5·61

The cation conductances decrease along the series $Me_4N^+ > Et_4N^+ > n\text{-}Bu_4N^+$; the anion conductances decrease slightly along the series $I^- > Br^- > ClO_4^-$, from which it would appear that the tetralkylammonium cations are practically unsolvated in ethylene carbonate, at least as regards the effective distance of closest approach of the ions.

The Walden's rule products, in Table 2, resemble similar products in other organic solvents, rather than the corresponding values in highly associated solvents such as water.

(2) *Conductivity of alkali-metal perchlorates in ethylene carbonate.*

Results.—The Λ_c–$\sqrt{c}$ plots for the alkali-metal perchlorates are shown in Fig. 2, and the results for one typical member of the series are given in Table 3; Λ_0 values obtained by Shed-

TABLE 3. *Conductivity of potassium perchlorate in ethylene carbonate at* 40°.

10^4c (mole l.$^{-1}$)	$10^2\sqrt{c}$	Λ_c (cm.^{2} ohm^{-1} g.-equiv.$^{-1}$)	10^4c (mole l.$^{-1}$)	$10^2\sqrt{c}$	Λ_c (cm.^{2} ohm^{-1} g.-equiv.$^{-1}$)	10^4c (mole l.$^{-1}$)	$10^2\sqrt{c}$	Λ_c (cm.^{2} ohm^{-1} g.-equiv.$^{-1}$)
0·7517	0·8670	41·69	4·0172	2·0043	41·32	8·0260	2·8330	41·05
1·1773	1·0850	41·64	4·3530	2·0865	41·31	8·2212	2·8673	41·04
1·6169	1·2715	41·56	4·8003	2·1910	41·25	8·9124	2·9854	41·00
2·4472	1·5644	41·47	5·3418	2·3112	41·21	11·0176	3·3193	40·88
2·5200	1·5874	41·47	6·0189	2·4534	41·18	12·4520	3·5288	40·80
3·4471	1·8569	41·37	6·1980	2·4891	41·17	13·7504	3·7082	40·75

TABLE 4.

Electrolyte	Λ_0	Slope (exptl.)	Slope (theor.)	$\frac{100\Delta \text{ Slope}}{\text{Theor. slope}}$	$\Lambda_0\eta$
$LiClO_4$	32·85	27·5	32·36	−15·1	0·607
$NaClO_4$	38·84	29·5	33·41	−11·7	0·719
$KClO_4$	41·99	33·2	33·96	−2·1	0·776
$RbClO_4$	42·59	34·5	34·06	+1·5	0·788
$CsClO_4$	43·59	35·9	34·24	+5·0	0·807

lovsky's extrapolation formula,[8] the theoretical and experimental Λ_c–$\sqrt{c}$ slopes, and the Walden product $\Lambda_0\eta$ are listed in Table 4.

[6] Fuoss and Accascina, *op. cit.*, ref. 4, pp. 107 *et seq.*
[7] Robinson and Stokes, "Electrolyte Solutions," 2nd edn., Butterworths, London, 1959, p. 408.
[8] Sears, Wilford, and Dawson, *J. Electrochem. Soc.*, 1956, **103**, 634.

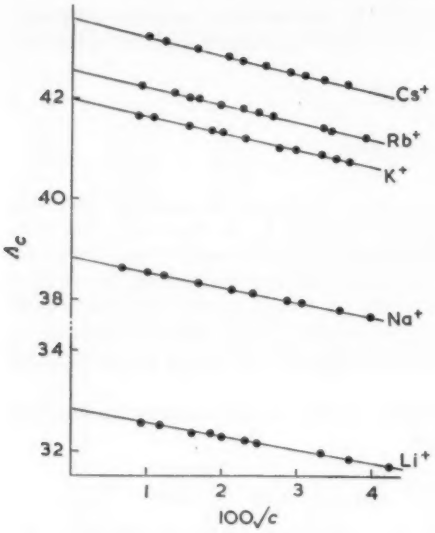

FIG. 2. *Equivalent conductances* Λ_c (*cm.*^{2} *ohm*$^{-1}$ *g.-equiv.*$^{-1}$) *of some alkali-metal perchlorates in ethylene carbonate at* 40°.

Discussion.—It is seen that the alkali-metal perchlorates are completely ionised in ethylene carbonate solution at 40°. The deviations of the Λ_c–$\sqrt{c}$ plots from the theoretical slopes change from −15·1% (for lithium perchlorate) to +5·0% (for cæsium perchlorate); we may compare these values with the corresponding percentage deviations of slope of the alkali-metal perchlorates in hydrogen cyanide [9] at 18°, and in *N*-methylacetamide [10] at 40°:

	Ethylene carbonate	Hydrogen cyanide	*N*-Methyl-acetamide
$LiClO_4$	−15·1	−16·6	—
$NaClO_4$	−11·7	−14·6	+4·0
$KClO_4$	−2·1	−0·94	+8·0

The alkali-metal halides show positive deviations of slope in hydrogen cyanide solution, the deviations decreasing from lithium to cæsium.

Negative deviations appear to be associated with large ions in a medium of high dielectric constant. Inclusion of the ion-size parameter a in equation (2) leads to the extended form:

$$\Lambda_c = \Lambda_0 - (26{\cdot}61 + 0{\cdot}175\Lambda_0)\sqrt{c}/(1 + \beta a) \quad . \quad . \quad . \quad . \quad (6)$$

where β was defined in equation (5); the following a parameters would account for the observed slopes in ethylene carbonate solution, the values in parentheses being the corresponding a-parameters for these salts in hydrogen cyanide solution:

	$LiClO_4$	$NaClO_4$	$KClO_4$
a (Å)	16·8 (18·6)	13·6 (15·0)	3·15 (1·17)

Whilst the results are not considered to be a very reliable estimate of the sum of the radii of the (solvated) ions, yet they indicate that the Li^+ and Na^+ ions are extensively

[9] Coates and Taylor, *J.*, 1936, 1245.
[10] Dawson, Wilhoit, Holmes, and Sears, *J. Amer. Chem. Soc.*, 1957, **79**, 3004.

solvated in ethylene carbonate and hydrogen cyanide solutions, in agreement with the decrease in equivalent conductance along the series:

$$(Cs^+ > Rb^+)^* > K^+ > Na^+ > Li^+.$$

Unfortunately, the limited solubility of alkali-metal salts in ethylene carbonate does not permit an extended concentration range to be studied. A more reliable series of ionic radii for the alkali-metal ions in ethylene carbonate is evaluated below.

On the other hand, the positive deviation in slope, observed for cæsium perchlorate, might be accounted for by ion-association; on this basis, the value of the ion-pair dissociation constant $K_{40°} = 0{\cdot}67 \pm 0{\cdot}05$ has been obtained for this electrolyte.

The Walden's rule products are similar to those of the tetra-alkylammonium halides and perchlorates in this solvent.

If we assume the tetra-alkylammonium ions to be unsolvated, and that the conductance of the perchlorate ion is independent of the cation present in ethylene carbonate solution, we can estimate the effective radii of the alkali-metal ions in this solvent. Taking the following radii (r in Å) for the tetra-alkylammonium cations:[11] NMe_4^+ 3·47; NEt_4^+ 4·00, NBu_4^+ 4·94, and interpolating the equivalent conductances Λ_0 of the alkali-metal perchlorates on the graph of Λ_0 against ionic radii for the tetra-alkylammonium perchlorates, we estimated the effective ionic radii of the alkali-metal cations, and the solvent molar volume at 40° being taken as 110 Å^3, the solvation number n was obtained:

	Li^+	Na^+	K^+	Rb^+	Cs^+
$r^+ =$	5·31	4·61	4·03	3·90	3·63
$n =$	6	4	2·5	2·2	1·7

The Walden product $\Lambda_0\eta$ has the value 0·294 for the tetraethylammonium cation in a number of different organic solvents;[12] assuming this value in ethylene carbonate, we may derive the following approximate ionic conductances in this solvent:

	Li^+	Na^+	K^+	Rb^+	Cs^+	NMe_4^+	NEt_4^+	NBu_4^+	ClO_4^-	Br^-	I^-
$\lambda°$	7	13	15	16	17	18	(15·8)	10	26	26·5	27

These values are consistently higher than the conductances in *N*-methylacetamide[10] at 40°, *viz.*,.

	Na^+	K^+	NMe_4^+	NEt_4^+	NBu_4^+	ClO_4^-	I^-
$\lambda°$	8·2	8·4	12·0	11·6	7·8	16·8	14·6

This is to be expected from the higher viscosity of the solvent: $\eta_{40°} = 0{\cdot}302$ poise.

We conclude that ethylene carbonate is a good ionising solvent for the alkali-metal perchlorates, and for the tetra-alkylammonium halides.

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[*Received, April 13th*, 1960.]

* These perchlorates have not been investigated in hydrogen cyanide solution.

[11] Robinson and Stokes, ref. 7, p. 125.
[12] Uhlich and Burr, *Z. angew. Chem.*, 1928, **41**, 443.

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22. *Infrared Spectra of Aryl Carboxylic Acids and Their Esters.*

By C. J. W. Brooks, G. Eglinton, and J. F. Morman.

Regularities in carbonyl stretching frequencies for the series Ar·COX [X = Me, OH (dimer), H, OEt, OMe, and OH (monomer)] are briefly discussed. Data (ν, $\Delta\nu_{\frac{1}{2}}^{a}$, and ε_a) are presented for the carbonyl and hydroxyl stretching vibrations of 21 monosubstituted methyl benzoates and 23 monosubstituted benzoic acids in dilute solution (carbon tetrachloride). The frequency data for *meta*- and *para*-substituted derivatives correlate well with the relative acidity values reported by Davis and Hetzer.[1]

Methyl *o*-halogeno- and *o*-methoxy-benzoates and the corresponding acids exhibit split carbonyl bands, ascribed to conformational isomerism rather than to Fermi resonance. Selected compounds have been studied in several solvents (n-hexane, carbon disulphide, chloroform, acetonitrile, and ether–carbon tetrachloride).

This paper reports part of a general attempt to relate spectroscopic data to molecular structures and conformations. It describes infrared spectroscopic studies of a series of monosubstituted benzoic acids and the corresponding methyl esters. Previous investigations include those of Flett,[2] Goulden,[3] O'Sullivan and Sadler,[4] and Thompson and his

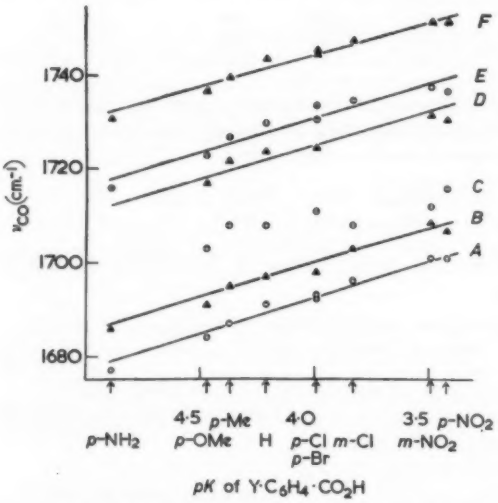

Fig. 1. *Carbonyl stretching frequencies* (CCl_4) *of* Y·C_6H_4·COX, *and* (*abscissa*) pK_a *of* Y·C_6H_4·CO_2H (*ref.* 1). (*A*) *Aryl methyl ketones* (X = Me).[a,b] (*B*) *Aryl carboxylic acids* (X = OH: *dimers*).[b] (*C*) *Aryl aldehydes* (X = H).[b] (*D*) *Ethyl esters of aryl carboxylic acids* (X = OEt).[b] (*E*) *Methyl esters of aryl carboxylic acids* (X = OMe).[b] (*F*) *Aryl carboxylic acids* (X = OH: *monomers*).[b]

[a] Jones, Forbes, and Mueller, *Canad. J. Chem.*, 1957, **35**, 504. [b] Present work.

co-workers.[5,6] Peltier *et al.*[7] have recently reported frequency data for some of the compounds examined: the complex absorption now shown to be exhibited by certain *ortho*-substituted benzoates was not disclosed by their work or by that of Forbes, Knight, and Coffen.[8]

It is well known that carbonyl stretching vibrations can be treated as dependent

[1] Davis and Hetzer, *J. Res. Nat. Bur. Stand.*, 1958, **60**, 569.
[2] Flett, *Trans. Faraday Soc.*, 1948, **44**, 767.
[3] Goulden, *Spectrochim. Acta*, 1954, **6**, 129.
[4] O'Sullivan and Sadler, *J.*, 1957, 2839.
[5] Thompson, Needham, and Jameson, *Spectrochim. Acta*, 1957, **9**, 208.
[6] Krueger and Thompson, *Proc. Roy. Soc.*, 1959, *A*, **250**, 22.
[7] Peltier, Pichevin, Dizabo, and Josien, *Compt. rend.*, 1959, **248**, 1148; Josien, Peltier, and Pichevin, *ibid.*, 1960, **250**, 1643.
[8] Forbes, Knight, and Coffen, *Canad. J. Chem.*, 1960, **38**, 728.

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principally on the immediate environment of the group concerned.[9] From Fig. 1, in which correlations of the type due to Fuson, Josien, and Shelton,[10] Thompson *et al.*,[5] and Peltier *et al.*[7] are applied to our data, it is clear that the frequency separations (in carbon tetrachloride) between an aryl methyl ketone (Ar·COMe) and the corresponding compounds of the types $(Ar{\cdot}CO_2H)_2$, $Ar{\cdot}CO_2Et$, $Ar{\cdot}CO_2Me$, and $Ar{\cdot}CO_2H$ remain essentially constant at 7, 34, 39, and 52 cm.$^{-1}$, respectively, in the group of *meta*- and *para*-substituted derivatives considered. Systematic deviations from linearity, disclosed by the data now determined, are ascribed to factors (*e.g.*, the varying effects of solvation) tacitly assumed constant in plotting ν_{OO} (CCl_4) against pK (aqueous). The marked elevation of frequency in monomeric carboxylic acids as compared with the methyl ketones may be attributed to the strong electron-withdrawing power of the hydroxyl group.[11]

Experimental

Materials.—Most of the acids were obtained commercially. 6-Chlorosalicylic acid was kindly supplied by Dr. J. F. J. Dippy. *o*-Allyloxybenzoic acid, m. p. 58—59°, was prepared according to Nummy and Tarbell's directions [12] and *o*-hydroxymethylbenzoic acid, m. p. 131—133°, from phthalide. Methyl esters were prepared with diazomethane. All samples were carefully purified, finally by sublimation or short-path distillation at 0·1 mm. (with the exception of *o*-hydroxymethylbenzoic acid). M. p.s of solids agreed with recorded values,[13] except that of methyl *p*-chlorobenzoate (34—35°; lit.,[13] 44°). The purity of all liquid samples and of methyl *p*-chlorobenzoate was checked by gas–liquid chromatography using the Pye "Argon Chromatograph." Columns (46″ × 1/5″) were of Apiezon L (5%) on Celite 545 (120—150 mesh). Column temperature was 175°, flow rate 35 ml./min., and exit pressure 760 mm. Carbon tetrachloride, carbon disulphide, and n-hexane (all "AnalaR") were used without purification. Chloroform ("AnalaR") was freed from ethanol by two successive passages through blue silica gel immediately before use. The ether (sodium-dried)–carbon tetrachloride solutions were examined immediately after preparation. Acetonitrile was purified by successive prolonged treatments with potassium hydroxide, calcium chloride, and phosphorus pentoxide, followed by distillation.

Measurements.—Spectra were recorded linearly in cm.$^{-1}$ as percentage transmission with a Unicam S.P. 100 double-beam infrared spectrometer equipped with an S.P. 130 sodium chloride prism-grating double monochromator [1500 lines per inch (650—2000 cm.$^{-1}$) and 3000 lines per inch (2000—3656 cm.$^{-1}$)] operated under dry-air conditions. Below 650 cm.$^{-1}$ the instrument was operated as a potassium bromide prism monochromator. The cell-well temperature was 29° ± 3°. The wave-number scale was calibrated against methane, water vapour, carbon dioxide, and ammonia.[14] The calibration was checked before and after each uninterrupted group of measurements by using the water vapour bands at 3566 and 3586 cm.$^{-1}$ and a solution of acetone in carbon tetrachloride (band at 1719 cm.$^{-1}$). Measurements are believed accurate to ±1 cm.$^{-1}$. The linearity of the percentage transmission scale was checked by Shrewsbury's procedure,[15] and all intensity measurements were made on bands of at least 10% transmission. The theoretical spectral slit-width, computed from tables supplied by Messrs. Unicam Instruments Ltd., was approximately 4 cm.$^{-1}$ at 3500 cm.$^{-1}$, 4·5 cm.$^{-1}$ at 1650 cm.$^{-1}$, 5·2 cm.$^{-1}$ at 1750 cm.$^{-1}$, and 4 cm.$^{-1}$ at 650 cm.$^{-1}$. Carbonyl and hydroxyl bands were scanned at 18 cm.$^{-1}$ per min. for carbon tetrachloride, carbon disulphide, and chloroform solutions, and at 12 cm.$^{-1}$ per min. for ether–carbon tetrachloride, n-hexane, and acetonitrile solutions. The region 400—700 cm.$^{-1}$ was scanned at 27 cm.$^{-1}$ per min. The frequency values given are the mean of at least two determinations. Unless specified otherwise peaks are symmetrical: the apparent half-band widths ($\Delta\nu_{\frac{1}{2}}^{a}$) are quoted to the nearest integer. Intensities are given as apparent extinction coefficients ϵ_a (l. mole^{-1} cm.$^{-1}$) rounded to the nearest 5 units and measured from

[9] Hartwell, Richards, and Thompson, *J.*, 1948, 1436; Bellamy, "The Infrared Spectra of Complex Molecules," Methuen & Co. Ltd., London, 2nd edn., 1958, Chapter 23.
[10] Fuson, Josien, and Shelton, *J. Amer. Chem. Soc.*, 1954, **76**, 2526.
[11] Taft, *J. Chem. Phys.*, 1957, **26**, 93.
[12] Nummy and Tarbell, *J. Amer. Chem. Soc.*, 1951, **73**, 1500.
[13] Heilbron and Bunbury, "Dictionary of Organic Compounds," Eyre and Spottiswoode, London, revised edition, 1953.
[14] Downie, Magoon, Purcell, and Crawford, *J. Opt. Soc. Amer.*, 1953, **43**, 941.
[15] Shrewsbury, "Unicam Spectrovision," 1958, No. 6, 1.

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a solvent–solvent base-line superimposed on the record of the absorption of the solution (determined with solvent in the reference beam). Full spectra (3650—400 cm.$^{-1}$) of certain substituted methyl benzoates will appear in the D.M.S. Index (Butterworths) as spectral cards numbers 6227 onwards.

Results and Discussion

Methyl Esters.—The results (CCl_4) are collected in Table 1. Single bands have been reported for *ortho*-substituted methyl [7] and ethyl [6] benzoates. With improved resolution it is now found that, while methyl *o*-methyl-, *o*-nitro-, and *o*-acetoxy-benzoate exhibit single sharp peaks, methyl *o*-halogeno-, *o*-methoxy-, and *o*-allyloxy-benzoates present two carbonyl bands separated to various degrees. This is not due to intermolecular effects, since dilution studies have shown that the relative intensities of the bands are independent of concentration. The band splitting observed in carbon tetrachloride solutions is more clearly defined in hexane (Fig. 2 and Table 2).

Of the two explanations which merit consideration for these effects, *viz.*, conformational equilibria or Fermi resonance, we favour the former in view of the evidence adduced below

Table 1. *Methyl esters of monosubstituted benzoic acids (in* CCl_4*).*[b]

	m- and *p*-Substituents					*o*-Substituents			
No.		ν_{CO}	$\Delta\nu_{\frac{1}{2}}$[a]	ε_a	No.		ν_{CO}	$\Delta\nu_{\frac{1}{2}}$[a]	ε_a
1	*m*-NMe_2	1727	15	680	13	*o*-OMe	(1745sh) †	*	*
							1736	*	430
							1718	(25)	265
2	*m*-OMe	1728	15	660					
3	None	1730	11	900	14	*o*-Allyloxy	(1748sh) †	*	*
							1737	*	450
							1718	(23)	260
4	*m*-F	1733	11	795	15	*o*-Me	1728	13	710
5	*m*-Cl	1735	11	915	16	*o*-F	1741	(12)	315
							1726	14	510
6	*m*-Br	1734	11	850					
7	*m*-NO_2	1738	10	890	17	*o*-Cl	1744	13	410
							1727	(22)	240 †
8	*p*-OMe	1723	16	725	18	*o*-Br	1744	12	465
							1727sh	*	(195) †
9	*p*-F	1732 ‡	11	775					
10	*p*-Cl	1731	11	920	19	*o*-I	1740	12	550
							(1727sh)	*	(160) †
11	*p*-Br	1734 ‡	12	820	20	*o*-NO_2	1747	14	710
12	*p*-NO_2	1737	12	750	21	*o*-OAc[c]	1733	12	865

Compounds Nos. 4, 5, 9, and 10 showed $\nu_{max.}$ in CS_2 1—2 cm.$^{-1}$ lower than the values for CCl_4 solutions, with $\Delta\nu_{\frac{1}{2}}$ 9 ± 1 cm.$^{-1}$. Values in parentheses are approximate. sh = shoulder.
* Not measured. † Estimated by band reflection. ‡ Unsymmetrical band.
[b] Measured as approximately 0·0015M-solutions in 5 mm. cells. [c] Acetate-carbonyl absorption at 1775 cm.$^{-1}$ ($\Delta\nu_{\frac{1}{2}}$, 16; ε_a, 530).

(see p. 114). We accordingly assign the band near 1730 cm.$^{-1}$ in the *o*-halogenobenzoates to conformation (Ia; X = Hal), and that near 1740 cm.$^{-1}$ to (Ib; X = Hal). (The ester group is depicted in the normally preferred conformation.[16]) Coplanarity of the substituents and the nucleus is not implied in these representations, the precise definition of which must await further evidence (*e.g.*, dipole-moment data). The higher-frequency band is associated with the alignment of carbonyl and C–halogen dipoles by analogy with α-halogeno-carbonyl compounds (*e.g.*, ketones,[17] aldehydes,[18] and esters [17,19,20]). The changes in the relative intensity of the two bands through the series *o*-F to *o*-I are most

[16] Mizushima, "Structure of Molecules and Internal Rotation," Academic Press Inc., New York, 1954, pp. 88, 89.
[17] Bellamy and Williams, *J.*, 1957, 4294.
[18] Bellamy and Williams, *J.*, 1958, 3465.
[19] Josien and Calas, *Compt. rend.*, 1955, **240**, 1641; Josien and Castinel, *Bull. Soc. chim. France*, 1958, 801.
[20] Brown, *J. Amer. Chem. Soc.*, 1958, **80**, 3513.

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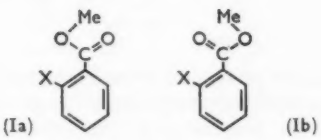
TABLE 2. *Methyl benzoate, methyl o-methoxybenzoate, and methyl o-halogenobenzoates in various solvents.*

Solvent	No.	Subst.	Absorption bands in carbonyl region: ν_{CO}	$\Delta\nu_{\frac{1}{2}}$ [a]	ε_a	ν_{CO}	$\Delta\nu_{\frac{1}{2}}$ [a]	ε_a
n-Hexane [b]	3	None	—	—	—	1735	9	1035
	13	*o*-OMe	1745	14	395	1723	16	305
	16	*o*-F	1749	9	260	1731	9	425
	17	*o*-Cl	1750	8	465	1733	14	285
	18	*o*-Br	1750	8	550	1735	18	240 †
	19	*o*-I	1746	8	630	1736sh	*	(200) †
Acetonitrile [c]	3	None	—	—	—	1724	11	790
	13	*o*-OMe	1731	16	505	(1709sh)	*	(105) †
	16	*o*-F	1733	12	520	1723	13	425 †
	17	*o*-Cl	1736	18	480	(1724sh)	*	(120) †
	18	*o*-Br	1737	(16)	535	(1729) §	*	(135) †
	19	*o*-I	1733	(15)	540	(1725) §	*	(85) †
Carbon disulphide [d]	3	None	—	—	—	1728	8	*
	13	*o*-OMe	1735	(15)	*	1713	24 †	*
	16	*o*-F	1739	(11)	*	1724	12	*
	17	*o*-Cl	1743	(13)	*	1726	(16)	*
	18	*o*-Br	1741	11 †	*	(1725) §	*	*
	19	*o*-I	1738	9 †	*	(1725) §	*	*

— No band present. § Concealed band. For other symbols see Table 1.
[b] *Ca.* 0·0076M-, [c] *ca.* 0·019M-, [d] *ca.* 0·015M-solutions; all in 0·5 mm. cells.

simply rationalised (the intensities being taken as approximately indicative of concentrations) in terms of the size of the halogen atom, the small fluorine atom permitting a preponderance of (I*a*; X = F) in the equilibrium mixture. For methyl *o*-methoxybenzoate in hexane the bands at 1723 and 1745 cm.$^{-1}$ are ascribed to conformations (Ia and Ib; X = OMe) respectively by analogy with the *o*-halogeno-esters and with the assignments made by T. L. Brown [20] for ethyl ethoxyacetate.

Additional support for the conformational assignments made for the *o*-halogeno- and *o*-methoxy-benzoates was derived from measurements in acetonitrile (Table 2 and Fig. 2). The carbonyl frequencies are generally about 6 cm.$^{-1}$ lower than in carbon tetrachloride. In each example, the intensity of the higher-frequency band is relatively higher in acetonitrile (and the lower-frequency band becomes less and less distinct in the series *o*-F, *o*-Cl, *o*-Br, and *o*-I; Fig. 2). Bellamy and Williams [17] observed a similar effect in α-chloroketones, and pointed out that intensification of the higher-frequency band in the more polar solvent supported its assignment to the more polar conformation. Brown [20] has reported similar results for ethyl chloro- and dichloro-acetate in chloroform and acetonitrile as compared with carbon tetrachloride.



(Ia) (Ib)

Methyl *o*-nitrobenzoate shows only a single (slightly unsymmetrical) band in the carbonyl region. Possibly in this ester the methoxycarbonyl group is so displaced by the preferential coplanarity of the nitro-group that there is essentially only one conformation. Single bands are exhibited by methyl *o*-toluate and *o*-acetoxybenzoate. Evidently these weakly polar substituents do not induce markedly different ν_{CO} values in the two possible conformations (cf. ref. 21). Two disubstituted esters have been briefly examined. Methyl 2,6-dimethoxybenzoate shows a single carbonyl band in n-hexane (1750 cm.$^{-1}$; $\Delta\nu_{\frac{1}{2}}$[a]

[21] Jones, Forbes, and Mueller, *Canad. J. Chem.*, 1957, **35**, 504; Jones, *Proc. Roy. Soc. Canada*, 1958, **52**, Ser. III, Sect. III, 9.

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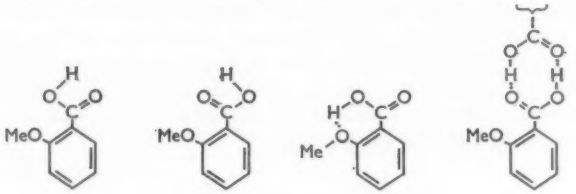
8 cm.$^{-1}$) and in carbon tetrachloride (1723 cm.$^{-1}$; $\Delta\nu_{\frac{1}{2}}^{a}$ 17 cm.$^{-1}$; ε_a 745). The remarkable solvent effects on the frequency and half-band width are presumably associated with the steric strain in this ester. Methyl 2,3-dimethoxybenzoate shows the expected split carbonyl band in n-hexane (1743 cm.$^{-1}$, $\Delta\nu_{\frac{1}{2}}^{a}$ ~11 cm.$^{-1}$, ε_a 440; 1729 cm.$^{-1}$, ε_a ~175) and, less clearly resolved, in carbon tetrachloride (1736 cm.$^{-1}$, $\Delta\nu_{\frac{1}{2}}^{a}$ ~18 cm.$^{-1}$, ε_a ~435; ~1721 cm.$^{-1}$, ε_a ~130) and in acetonitrile (1730 cm.$^{-1}$, $\Delta\nu_{\frac{1}{2}}^{a}$ ~16, ε_a 495; 1719 cm.$^{-1}$, ε_a ~95).

With regard to the intensities of carbonyl bands in substituted methyl benzoates, the apparent half-band widths and extinction coefficients (Tables 1 and 2) show no striking variations. Integrated intensity values (A) computed by Ramsay's method [22] ranged from $2{\cdot}9 \times 10^4$ (No. 9) to $4{\cdot}1 \times 10^4$ l. mole^{-1} cm.$^{-2}$ (No. 8). The values are based on single determinations and show no regularity. Thompson *et al.*[5] have demonstrated a linear relation between log A (by area integration) and σ for a group of six *meta*- and *para*-substituted ethyl benzoates. That the *ortho*-substituted esters did not conform [6] is not surprising in view of the complex absorption now disclosed.

Substituted Benzoic Acids.—Data for *meta*- and *para*-substituted acids (Table 3) indicate that the monomer carbonyl band ranges from 1737 to 1752 cm.$^{-1}$ and the dimer band from 1691 to 1709 cm.$^{-1}$. In the hydroxyl region the monomer band position is dependent on the substituent (and can be related [3] to the pK of the acid—see also below), while the dimer band is remarkably constant in appearance throughout the series examined. Data for nine *ortho*-substituted acids are tabulated. Of these, *o*-toluic, *o*-nitrobenzoic, and *o*-acetoxybenzoic acid exhibit single monomer carbonyl bands. In *o*-methoxybenzoic acid [the conformation of CO_2H is written as in (II) following Mizushima; [16] Davies [23] has depicted a hydrogen bond between the carbonyl and hydroxyl groups] the occurrence of the three species (II) [the two possible forms (IIa) and (IIb) [24] being treated as one], (III), and (IV) was demonstrated spectroscopically by Fox and Martin,[25] who showed that the hydroxyl stretching frequencies due to forms (II), (III), and (IV) in carbon tetrachloride solution were 3530, 3362, and *ca.* 2950 cm.$^{-1}$, respectively. We assign the carbonyl absorption as follows: the predominant form (III), 1751 cm.$^{-1}$; (IV) (three possible conformations), approx. 1703 cm.$^{-1}$. The shoulder observed near 1760 cm.$^{-1}$ may be tentatively ascribed to the small amount of form (II). It seems probable that the principal conformation of the dimer is (IV), as discussed further below.

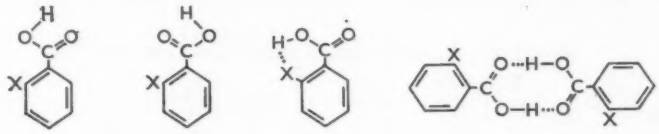


(IIa) (IIb) (III) (IV)

The series of *o*-halogeno-acids presents interesting features. The monomeric carbonyl bands parallel those of the methyl esters in showing two peaks. One is at a slightly lower frequency than that found for benzoic acid, the other is substantially higher. The separation of about 17 cm.$^{-1}$ between the peaks remains essentially constant throughout the series, but the relative intensities (ε_a) change progressively from *o*-F ($\varepsilon_{1755}/\varepsilon_{1739} = 0{\cdot}70$) to *o*-I ($\varepsilon_{1753}/\varepsilon_{1736} \approx 3{\cdot}3$), as indicated in Fig. 2. The attribution of both peaks to monomeric forms was confirmed in every case by dilution studies. In the hydroxyl absorption region the spectra of the *o*-halogeno-acids are almost indistinguishable from those of the *meta*- and *para*-isomers, except in the exact position of the monomer band near 3530 cm.$^{-1}$.

[22] Ramsay, *J. Amer. Chem. Soc.*, 1952, **74**, 72.
[23] Davies, in "Hydrogen Bonding," Pergamon Press, London, 1959, p. 393.
[24] Davies and Griffiths, *J.*, 1955, 132.
[25] Fox and Martin, *Nature*, 1939, **143**, 199.

The observed absorption bands near 1738 and 1755 cm.$^{-1}$ are consequently attributed to the conformational isomers (Va; X = Hal) and (Vb; X = Hal) and the absorption near 1700 cm.$^{-1}$ to the three possible dimeric forms derived therefrom. We believe that the dimers exist principally in the conformation (VI; X = Hal) since (i) the frequency



(Va) (lower-frequency band) (Vb) (higher-frequency band) (Vc) (VI)

separations between the carbonyl bands attributed to (Vb) and the corresponding dimer bands have values close to those (~45 cm.$^{-1}$) found for all the other substituted benzoic acids examined; (ii) in the crystalline state, *o*-chlorobenzoic and *o*-bromobenzoic acid exist as depicted in (VI), as demonstrated by *X*-ray crystallographic studies (personal communication from Dr. G. A. Sim and Mr. G. Ferguson, The Chemistry Department, Glasgow University). Solid state spectra of the acids were not informative.

Intramolecular hydrogen bonding (Vc; X = Hal) in *o*-halogenobenzoic acids has been frequently postulated (*e.g.*, refs. 1, 8, 26, but cf. 27). However, the single, closely similar monomer hydroxyl bands observed for the four *o*-halogeno-acids in carbon tetrachloride or chloroform solutions are incompatible with this proposal. [In the *o*-halogenophenols (hydrogen bond in 5-membered ring) ν_{OH} ranges [28] from 3584 (*o*-F) to 3500 (*o*-I) cm.$^{-1}$.] Possibly hydrogen bonding is inhibited in the *o*-halogeno-acids by steric displacement of the carboxyl group due to repulsion between the halogen and hydroxylic oxygen atoms. In support of this we note that in 6-chlorosalicylic acid, in which proximity and coplanarity of the halogen and hydroxylic oxygen atoms are both enforced by the chelation of the remaining groups, two bands, at 3508 cm.$^{-1}$ (free) and 3430 cm.$^{-1}$ (bonded), are observed.

Absorption data for solutions of *o*-methoxybenzoic acid and of the *o*-halogenobenzoic acids in chloroform and in mixtures of ether and carbon tetrachloride are recorded in Tables 4 and 5. The splitting of the monomer carbonyl absorption is not obvious in chloroform (*e.g.*, Fig. 3), an effect partly attributable to the usual band-broadening induced by this solvent. The molecular species involved are doubtless solvated monomers, since the frequencies are markedly displaced (−7 to −17 cm.$^{-1}$) from those observed in carbon tetrachloride, whereas the dimer absorption frequencies are almost unaltered. The monomer frequency shifts (ν_{CO} in CCl_4 minus ν_{CO} in $CHCl_3$) are of the same order as those we have observed for substituted methyl benzoates (*p*-NO_2, −11; *p*-Cl, −9; unsubstituted, −10; *m*-NMe_2, −10 cm.$^{-1}$: the effect of the substituents on the polarity of the carbonyl linkage is not evident). We regard the similarity of the dimer frequencies in chloroform and carbon tetrachloride as due to the virtual elimination of the basicity of the carbonyl group consequent upon dimer formation (cf. refs. 29, 30). Cole and Michell [31] have proposed an explanation based on steric shielding. The single frequencies recorded by O'Sullivan and Sadler [4] for these acids in chloroform appear to correspond approximately to our dimer frequencies.

The results for ether–carbon tetrachloride solutions (*e.g.*, Fig. 3) parallel those for

[26] Kilpatrick and Mears, *J. Amer. Chem. Soc.*, 1940, **62**, 3051; Ito, Tsukioka, and Imanishi, *ibid.*, 1960, **82**, 1559.
[27] McDaniel and Brown, *J. Amer. Chem. Soc.*, 1955, **77**, 3756.
[28] Baker, *J. Amer. Chem. Soc.*, 1958, **80**, 3598.
[29] Cannon, *Mikrochim. Acta*, 1955, 555.
[30] Bellamy and Williams, *Proc. Roy. Soc.*, 1960, *A*, **255**, 22.
[31] Cole and Michell, *J.*, 1959, 2005.

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carbon tetrachloride in respect of (i) the splitting of the monomer absorption bands [ether-bonded monomer ($Ar{\cdot}CO_2H \cdots OEt_2$) in this case], (ii) the frequency separation of about 16 cm.$^{-1}$ between the bands, and (iii) the change in relative intensities through the sequence *o*-F, *o*-Cl and *o*-Br. The frequency shifts (about 18 cm.$^{-1}$) parallel those observed for dioxan [32] as compared with carbon tetrachloride.[2] In both cases the effect is due to the

TABLE 3. *Monosubstituted benzoic acids (in* CCl_4*).*[b]

		Monomer			Dimer			Monomer [c,d]	
No.	Subst.	ν_{CO}	$\Delta\nu_{\frac{1}{2}}$[a]	ε_a	ν_{CO}	$\Delta\nu_{\frac{1}{2}}$[a]	ε_a	ν_{OH}	$\Delta\nu_{\frac{1}{2}}$[a]
22	*m*-NMe_2	1740	14	245	1693	15	660	3541	29
23	*m*-OMe	1741	13	215	1698	17	640	3539	30
24	*m*-Me	1742	13	260	1698	14	805	3540	27
25	None	1744	13	270	1697 ‡	16	750	3540	27
26	*m*-F	1748	11	270	1703	13	685	3536	30
27	*m*-Cl	1748	12	285	1703	16	700	3535	30
28	*m*-Br	1748	12	275	1702	14	685	3535	31
29	*m*-NO_2	1752	10	305	1709	18	575	3530	35
30	*p*-OMe	1737	13	*	1691	12	*	3542	25
31	*p*-Me	1740	12	265	1697 ‡	12	995	3541	26
32	*p*-F	1745	13	255	1699	12	880	3538	30
33	*p*-Cl	1745	11	*	1698 ‡	10	*	3536	32
34	*p*-Br	1746	13	*	1698	16	*	3536	32
35	*p*-NO_2	1752	13	*	1707	15	*	3529	*
36	*o*-OMe	(1760sh)	*	*	1702 ¶	*	*	3530	40
		1751	14	670				3365	80
37	*o*-Allyloxy	1751	15	880	1703	*	*	3529	38
								3354	90
38	*o*-Me	1742 ‡	16	250	1696 ‡	18	590	3538	30
39	*o*-F	1755	12	155	1707	23	535	3529	32
		1739	*	220	(1700sh)	*	*		
40	*o*-Cl	1756	12	200	1706	25	440	3527	38
		1738	*	(105) †					
41	*o*-Br	1757	12	200	1711 ‡	26	420	3528	38
		1738	*	(95) †					
42	*o*-I	1753	12	230	1708 ‡	22	465	3530	38
		(1736sh)	*	(90) †					
43	*o*-NO_2	1760	16	*	1715	19	*	3520	35
44	*o*-OAc [e]	1747 ‡	14	395	1702	18	545	3532	35

¶ Very weak band: $\nu_{max.}$ confirmed by measurement at higher concentration. For other symbols see Table 1.

[b] Measured as 0·00150 ± 0·00002M-solutions [except for Nos. 36 (0·0018M) and 30, 33, 34, 35, and 43 (saturated solutions)] in 5 mm. cells (ν_{CO}) or 20 mm. cells (ν_{OH}). [c] In the region 3650—2500 cm.$^{-1}$ the following additional assignments were made: No. 22, 2807 cm.$^{-1}$ (ν_{CH},NMe); [f] Nos. 23 and 30, 2835 and 2841 cm.$^{-1}$ respectively (ν_{CH},OMe). [g] No. 36 showed no sharply defined peak attributable to the latter vibration. Nos. 36 and 37 showed a weak band near 3475 cm.$^{-1}$ presumed to be the first overtone of the intense carbonyl band at 1751 cm.$^{-1}$. [d] ε_a for ν_{OH} was virtually constant at about 50 cm.$^{-1}$, except for Nos. 36 and 37 for which ε_a values were: No. 36, 15 and 100 cm.$^{-1}$; No. 37, 10 and 105 cm.$^{-1}$. [e] Acetate carbonyl at 1776 cm.$^{-1}$ ($\Delta\nu_{\frac{1}{2}}$ 15, ε_a 505). [f] Hill and Meakins, *J.*, 1958, 760. [g] Henbest, Meakins, Nicholls, and Wagland, *J.*, 1957, 1462.

mitigation of the electron-withdrawing character of the carboxylic OH group by hydrogen-bonding to the ether oxygen atom: the frequencies of carbonyl groups *per se* are only slightly affected by ether as compared with carbon tetrachloride [*e.g.*, acetophenone, 1694 (ether) and 1692 (carbon tetrachloride) cm.$^{-1}$].[30] Cole and Michell [31] have reported for benzoic acid, in dioxan, carbonyl bands at 1723 and 1636 cm.$^{-1}$, which they ascribe respectively to monomer and to a hydrogen-bonded benzoic acid–dioxan complex. We observe no carbonyl band near 1636 cm.$^{-1}$ for benzoic acid in ether–carbon tetrachloride: the absorption reported is probably a result of loss of spectrometer energy by solvent absorption. We assign the band at 1723 cm.$^{-1}$ to the dioxan-bonded monomeric acid. In Table 5 data are recorded for the carbonyl absorption of *o*-methoxybenzoic acid in ether–carbon tetrachloride. With increasing concentrations of ether the intensity of the band

[31] Flett, *J.*, 1951, 962.

FIG. 2. *Carbonyl absorptions of benzoic acid, methyl benzoate and o-substituted derivatives in various solvents.* (A) CCl_4; (B) $CHCl_3$; (C) *n-hexane*; (D) MeCN. *The relevant concentrations and path lengths are as given in Tables* 1, 2, *and* 3 *except for B* (0·0015M-*solution in* 5 *mm. cells*).

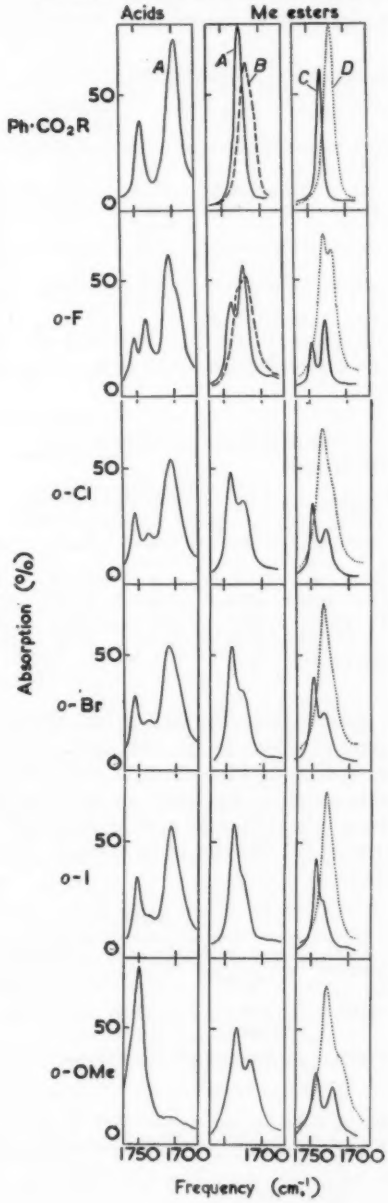


FIG. 3. *Carbonyl absorption of o-fluorobenzoic acid in* (*A*) CCl_4, (*B*) 8% (v/v) *ether*–CCl_4, *and* (*C*) $CHCl_3$. *Solutions are* 0·0015M *in* 5 *mm. cells.*

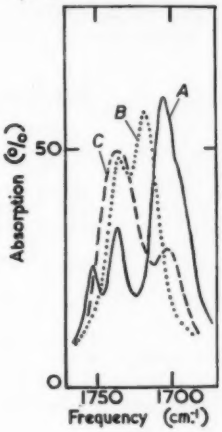
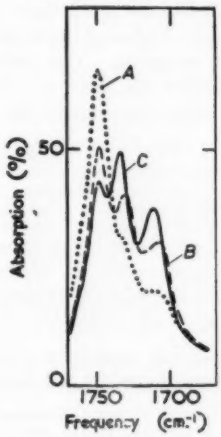


FIG. 4. *Carbonyl absorption of o-methoxybenzoic acid in ether*–CCl_4 *mixtures.* (*A*) 0·0015M *in* 4% (v/v) Et_2O–CCl_4: 5 *mm. cells.* (*B*) 0·015M *in* 20% (v/v): 0·5 *mm.* (*C*) 0·015M *in* 100% Et_2O: 0·5 *mm.*



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associated with the intramolecularly bonded conformation (III) is markedly reduced, finally to less than half the value in carbon tetrachloride. Fig. 4 illustrates the latter trend and also shows the emergence of two new carbonyl bands (at approximately 1715 and 1735 cm.$^{-1}$). These are attributed to the ether-bonded forms corresponding to the two conformations (IIa) and (IIb). The possibility that the band near 1715 cm.$^{-1}$ is due to a dimeric form is rejected since it increases in intensity with increasing ether concentration.

At approximately equimolar concentrations the ratio of monomer to dimer increases

TABLE 4. *Benzoic acid and o-substituted benzoic acids.*[b]

		Chloroform							Ether–CCl_4 (20 : 80 v/v)		
		Monomer			Dimer			Monomer	Bonded monomer		
No.	Subst.	ν_{CO}	$\Delta\nu_{\frac{1}{2}}$[a]	ε_a	ν_{CO}	$\Delta\nu_{\frac{1}{2}}$[a]	ε_a	ν_{OH}	ν_{CO}	$\Delta\nu_{\frac{1}{2}}$[a]	ε_a
25	None	1734	25	360	1697	20	235	3524	1726	15	720
39	*o*-F	1738	34	375	1706	(25)	(195)	3514	1737	17	355
									1721	17	485
40	*o*-Cl	1744 ‡	30	380	1706	(28)	(170)	3512	1738	14	465
									1720	*	(190) †
41	*o*-Br	1743	25	395	1706	(24)	(160)	3512	1737	13	450
									(1722sh)	*	(150) †
42	*o*-I	1746 ‡	30	355	1709	(38)	(155)	3509	*	*	*
45	*o*-CH_2OH	1721	*	*	1687	*	*	3515	*	*	*

For symbols see Table 1. [b] Measured as 0·0015M-solutions in 5 mm. cells ($CHCl_3$), except No. 45 (saturated solution), and in 2 mm. cells (ether–CCl_4).

TABLE 5. *Carbonyl bands of monomeric forms of* o-*methoxybenzoic acid in ether–carbon tetrachloride.*

			Monomer (III)		Ether-bonded monomer (IIb)?		(IIa)?	
Molarity	Cell path (mm.)	Ether (% v/v)	ν_{CO}	ε_a	ν_{CO}	ε_a	ν_{CO}	ε_a
0·0018	5·0	0	1751	670	—	—	—	—
0·0015	5·0	4	1752	630	(1735sh)	*	(1710)	*
0·015	0·5	20	1751	405	1734	(265)	1712	(205)
0·015	0·5	50	1751	(325)	1735	(345)	1714	(240)
0·015	0·5	100	1752	(315)	1738	(385)	1715	(260)

For symbols see Table 1.

through the sequence of solvents, n-hexane, carbon tetrachloride, carbon disulphide, chloroform, and acetonitrile. Even at high concentrations (~1M, 0·05 mm.) in acetonitrile, benzoic acid shows negligible dimer absorption. *o*-Fluorobenzoic acid gives two monomer carbonyl bands in n-hexane and in acetonitrile: in the latter solvent they are of equal intensity. The carbonyl absorption of *o*-methoxybenzoic acid is relatively unaffected by the solvent: this is explicable in terms of the stability of form (III). Typical data (wave-numbers in cm.$^{-1}$) are assembled below.

	Solvent				Solvent		
Sub-	n-Hexane		Acetonitrile	Sub-	n-Hexane		Acetonitrile
stituent	$\nu_{CO(monomer)}$	$\nu_{CO(dimer)}$	$\nu_{CO(monomer)}$ [a]	stituent	$\nu_{CO(monomer)}$	$\nu_{CO(dimer)}$	$\nu_{CO(monomer)}$ [a]
None ...	1750	1703	1727	*o*-I	*	*	1736
o-F	1762	1710	1738	*o*-OMe ...	1759	(1707)	1739
	1746	(1698sh)	1726		(1763sh)		

[a] Half-band widths ($\Delta\nu_{\frac{1}{2}}$) 20 ± 2 cm.$^{-1}$. Values in parentheses are approximate.
* Not measured. sh = shoulder.

Evidence relating to Conformational Assignments.—In recent papers [33,34] R. N. Jones and his colleagues have pointed out that solvent- and temperature-dependent modifications

[33] Angell, Krueger, Lauzon, Leitch, Noack, Smith, and Jones, *Spectrochim. Acta*, 1959, 926.
[34] Jones, Angell, Ito, and Smith, *Canad. J. Chem.*, 1959, **37**, 2007.

of carbonyl frequencies, though often attributed to conformational equilibria, can be produced by Fermi resonance and other vibrational interactions. The principal evidence in support of our conformational interpretations is as follows:

(*a*) The retention of regular absorption patterns (Figs. 2 and 3 and Tables 2, 3, and 4) by the methyl *o*-halogenobenzoates in n-hexane and carbon tetrachloride, and by the corresponding carboxylic acid monomers in carbon tetrachloride and ether–carbon tetrachloride, seem unlikely to result from Fermi resonance.

TABLE 6. *Frequency shifts* ($\Delta\nu = \nu_{hexane} - \nu_{solvent}$) *and approximate relative intensities of "split" carbonyl bands* [a] *in various solvents.*

	n-Hexane [d]		CCl_4 [e]		CS_2 [e]		MeCN [d]	
	ν	$\varepsilon_1/\varepsilon_2$	$\Delta\nu$	$\varepsilon_1/\varepsilon_2$	$\Delta\nu$	$\varepsilon_1/\varepsilon_2$	$\Delta\nu$	$\varepsilon_1/\varepsilon_2$
Methyl benzoate	1735	—	5	—	7	—	11	—
Methyl *o*-fluorobenzoate	1749	0·61	8	0·62	10	0·72	16	1·22
	1731		5		7		8	
Methyl *o*-chlorobenzoate	1750	1·64	6	1·70	7	1·70	14	4·0
	1733		6		7		9	
Methyl *o*-methoxybenzoate	1745	1·3	9	1·62	10	1·70	14	4·8
	1723		5		8		14	
Benzoic acid [b]	1750	—	6	—	9	—	23	—
o-Fluorobenzoic acid [b]	1762	0·71	6	0·70	9	0·73	24	1·0
	1746		5		8		20	
Coumarin	1759	3·2	4	0·84	6	0·75	4	0·26
	1746		3		5		11	
Cyclopentanone	1755	(15)	5	(7)	7	(7)	10	1
	1724 †		−3 †		−2 †		−11	
Cyclohexanone [c]	1724	—	5	—	7	—	15	—

[a] In the $\Delta\nu$ columns the upper figures refer to the higher-frequency bands ν_1. [b] Monomer bands. In 20% v/v ether–CCl_4 benzoic acid has $\Delta\nu = 24$ cm.$^{-1}$; *o*-fluorobenzoic acid has $\Delta\nu_1 = 25$, $\Delta\nu_2 = 25$ cm.$^{-1}$, and $\varepsilon_1/\varepsilon_2 = 0{\cdot}73$. The dimer carbonyl causes some interference in the hexane, CCl_4, and CS_2 solutions. [c] Data from ref. 33; $\Delta\nu$ values refer to $\nu_{cyclohexane}$. [d] 0·5 mm. cells. [e] 5 mm. cells.

(*b*) The regularly increasing preponderance of the higher frequency bands through the series of *ortho*-substituents H, F, Cl, Br, I parallels the trend already described in conformational terms for the *o*-halogenoacetophenones.[21] If Fermi resonance is invoked, *decreased* coupling would have to occur for a smaller frequency separation between the bands—the inverse of normal experience. Furthermore, there are no obvious frequencies (400 cm.$^{-1}$ upwards) which might be consistently employed to provide overtone or combination bands close to 1730 cm.$^{-1}$ in either the acids or their methyl esters.

(*c*) The solvent shifts (Table 6) of the split carbonyl bands in methyl *o*-fluoro-, *o*-chloro-, and *o*-methoxy-benzoates, and in *o*-fluorobenzoic acid, are not much different from the values observed for the unsubstituted compounds. On the other hand, in the examples (coumarin [34] and cyclopentanone [33,35]) ascribed to Fermi resonance, the solvent shifts are irregular, since neither of the observed fundamentals represents the simple carbonyl group frequency.[36] The ratio ($\varepsilon_1/\varepsilon_2$) of the intensities of the two bands (higher ν_1/lower ν_2) observed in Fermi resonance decreases markedly as the solvent polarity is increased. In the substituted benzoic acids and esters the reverse trend is clearly shown. Preliminary observations of the temperature dependence of the absorption of methyl *o*-fluorobenzoate in carbon tetrachloride indicate that, over the range 30—70°, the higher frequency band [attributed to (Vb; X = F)] becomes relatively more intense as the temperature rises: at 70° the ratio of intensities was 7% above that found at 30°, an effect consonant with our assignments. A study of deuterated compounds would be desirable.

(*d*) Where detectable conformational isomers are not expected, the carbonyl bands are

[35] Allen, Ellington, and Meakins, *J.*, 1960, 1909.
[36] Brand and Speakman, "Molecular Structure," Edward Arnold, London, 1960, p. 154.

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not split; *e.g.*, the *meta*- and *para*-substituted benzoic acids and esters and methyl 2,6-dimethoxybenzoate.

(*e*) Careful comparison of the spectra of the methyl *o*-halogenobenzoates as liquid films, and as solutions in carbon disulphide and acetonitrile, reveals that intensity changes parallel to those in the carbonyl region occur in at least two pairs of bands (near 1040 cm.$^{-1}$ and near 1260 cm.$^{-1}$) in the region 400—1600 cm.$^{-1}$. This behaviour is entirely consistent with the presence of two isomers. The *m*- and *p*-halogenobenzoates do not show these effects.

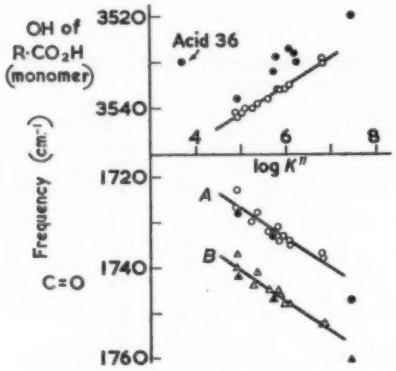

FIG 5. *Carbonyl and hydroxyl stretching frequencies* (CCl_4) *of aryl carboxylic acids and methyl esters, and* (*abscissa*) log K'' *for the neutralisation of the acids by diphenylguanidine in benzene* (*ref.* 1).

●▲: ortho-*Substituted derivatives.*

A, R·CO_2Me; *B*, R·CO_2H (*monomer*).

Correlation of Frequencies with Acid Strengths.—Davis and Hetzer [1] have suggested that frequency data determined in relatively non-polar solvents might be better correlated with comparative acid strengths determined in similar solvents than with aqueous p*K*'s. A plot of this type is presented in Fig. 5. The monomer hydroxyl frequencies of the *meta*- and *para*-substituted acids are well accommodated, but the values for *ortho*-substituted acids are displaced, mostly to lower frequencies. We conclude that, although the use of non-aqueous acid strengths might appear desirable, yet it does not in this instance greatly improve the consistency already shown by the p*K* or σ values.

Plotting [2 log ε_a (monomer) — log ε_a (dimer)] against log *K*'' affords evidence of a linear relation, in accordance with correlations previously suggested [37,1] between the equilibrium constants for dimer dissociation and for ionisation.

We thank Professor R. A. Raphael and Dr. J. Reid for their interest, Drs. L. J. Bellamy and J. C. D. Brand for advice, Miss J. S. Young for preparing many of the samples examined, and Mrs. F. Lawrie and Miss P. Pellitt for some measurements.

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[*Received, June 7th*, 1960.]

[37] Allen and Caldin, *Quart. Rev.*, 1953, **7**, 255.

23. *The Reactions of Sodium Ethyl Xanthate with Ethanol and with Water.*

By G. INGRAM and B. A. TOMS.

Sodium ethyl xanthate is shown to react with both ethanol and water by addition to the thiocarbonyl linkage. With ethanol, the primary product, sodium di-*O*-ethyl dithio-orthocarbonate, yields diethyl thioncarbonate on mild oxidation and is converted into silver ethyl xanthate, or into diethyl carbonate and silver sulphide, by appropriate treatment with silver nitrate. With water, the initial production of *S*-sodium *O*-ethyl dihydrogen dithio-orthocarbonate enables silver salts of the $EtO{\cdot}COS_2^{3-}$ ion to be obtained in addition to silver ethyl xanthate. Thus a new interpretation of the behaviour of the xanthate ion in aqueous solution is presented.

WE have previously reported [1] that sodium trithiocarbonate reacts with ethanol to produce sodium ethyl xanthate and sodium hydrogen sulphide:

$$CS_3^{2-} + EtOH \longrightarrow EtO{\cdot}CS_2^- + HS^- \quad . . . . . (1)$$

This reaction, and our belief that it proceeds by the addition of ethanol to the thiocarbonyl linkage of the CS_3^{2-} ion, suggested that ethanol might react analogously with sodium *O*-ethyl xanthate. We have now proved this, although the new reaction, unlike (1), has to be promoted. The primary products are diethyl thioncarbonate and sodium hydrogen sulphide, and we consider that they are derived from sodium di-*O*-ethyl dithio-orthocarbonate:

$$EtO{\cdot}CS_2^- + EtOH \rightleftharpoons \left[\begin{matrix} EtO & & SH \\ & C & \\ EtO & & S \end{matrix}\right]^- \rightleftharpoons (EtO)_2CS + HS^- \quad . . . . (2)$$

This mechanism supports our previous suggestion that reaction (1) might proceed through disodium *O*-ethyl trithio-orthocarbonate:

$$CS_3^{2-} + EtOH \rightleftharpoons \left[\begin{matrix} EtO & & S \\ & C & \\ HS & & S \end{matrix}\right]^{2-} \longrightarrow EtO{\cdot}CS_2^- + HS^- \quad . . . . (3)$$

The discovery of reaction (2), and the knowledge that the trithiocarbonate ion reacts uniquely with water,[1] led us to investigate the primary reaction between sodium *O*-ethyl xanthate and water because earlier work,[2,3] particularly that of Makens,[4] had indicated that the hydrolysis of alkali-metal xanthates is not adequately represented by the simple equilibrium:

$$RO{\cdot}CS_2^- + H_2O \rightleftharpoons RO{\cdot}CS_2H + HO^- \quad . . . . . (4)$$

We now present new facts and argue that reaction (4) must be replaced by a more comprehensive concept based on the hydration of the xanthate ion. The essence of our hypothesis is that when sodium ethyl xanthate is dissolved in water, *S*-sodium *O*-ethyl dihydrogen dithio-orthocarbonate is produced and dissociates as follows:

$$EtO{\cdot}CS_2^- + H_2O \rightleftharpoons \left[\begin{matrix} EtO & & SH \\ & C & \\ HO & & S \end{matrix}\right]^- \underset{H^+}{\rightleftharpoons} [H(EtO{\cdot}COS_2)]^{2-} \underset{H^+}{\rightleftharpoons} EtO{\cdot}COS_2^{3-} \quad (5)$$

$$\left[\begin{matrix} EtO & & SH \\ & C & \\ HO & & S \end{matrix}\right]^- \overset{HO^-}{\rightleftharpoons} EtO{\cdot}CS_2H$$

These equilibria afford a rational basis for interpreting, and exploiting, the properties of sodium ethyl xanthate in aqueous media, and some examples are given here. Thus,

[1] Ingram and Toms, *J.*, 1957, 4328.
[2] Schaum, Siedler, and Wagner, *Kolloid-Z.*, 1932, **58**, 341.
[3] Klauditz, *Papier-Fabr.*, 1939, **37**, 251.
[4] Makens, *J. Amer. Chem. Soc.*, 1935, **57**, 405.

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although *O*-ethyl dithio-orthocarbonic acid itself is unknown and is presumed to be highly unstable,[5] we believe that we have obtained the silver salts from the $[H(EtO{\cdot}COS_2)]^{2-}$ and $EtO{\cdot}COS_2^{3-}$ ions, although the latter product was originally regarded [4] as an equimolar mixture of silver ethyl monothiocarbonate and silver sulphide.

The hydration of the xanthate ion recalls (and supports) our previous suggestion that the hydrolysis of sodium trithiocarbonate might be effected by the formation and decomposition of di-*S*-sodium dihydrogen trithio-orthocarbonate: [1]

$$CS_3^{2-} + H_2O \rightleftharpoons \left[\begin{matrix} HO \\ HS \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} S \\ S \end{matrix}\right]^{2-} \rightleftharpoons HCOS_2^- + HS^- \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Thus the reactions of both sodium *O*-ethyl xanthate and sodium trithiocarbonate with both ethanol and water can all be shown to depend upon the addition of a molecule of the reactant to the thiocarbonyl linkage. There is evidence that this mechanism may also be applicable to the reactions of primary amines with metal xanthates and dithiocarbamates.

Experimental

Materials.—Ethanol was generally " absolute alcohol B.P.," and anhydrous ethanol was obtained from this by Lund and Bjerrum's method; [6] light petroleum (b. p. 34·0—35·0°) was fractionated from " AnalaR " light petroleum (b. p. 30—40°). Other materials were of " AnalaR " quality or as specified previously.[1]

Gas Analysis.—Hydrogen sulphide, carbon dioxide, carbonyl sulphide, and carbon disulphide were swept from a reaction mixture by a stream of nitrogen which then passed through bubblers containing selectively absorbent liquids.[1] Carbonyl sulphide was collected in the bubblers intended for carbon dioxide and carbon disulphide respectively. The amount trapped by the aqueous sodium hydroxide was estimated by adding an excess of lead acetate–acetic acid reagent,[1] immediately after the residual sodium hydroxide had been titrated,[7] and then weighing the lead sulphide which was produced overnight; the original carbon dioxide estimation was then corrected accordingly. Carbonyl sulphide trapped by the ethanolic sodium hydroxide was estimated differentially by treating two aliquot parts as follows: (i) the combined amounts of carbonyl sulphide and carbon disulphide were determined iodometrically; (ii) after neutralization with acetic acid, thallous ethyl xanthate was precipitated and weighed (thallous ethyl monothiocarbonate is soluble in both ethanol and water).

Gas–Liquid Chromatography.—This method was used to detect diethyl carbonate and diethyl thioncarbonate, singly and together, in carbon tetrachloride solution and to check the purity of specimens of diethyl thioncarbonate.

A " V.P.C. Apparatus Mk. II," manufactured by Messrs. Griffin & George (London), was available. This relied on a thermal-conductivity detector and was operated at maximum sensitivity with bridge current 100 mA; the chart speed was 6 in./hr. The column, of glycerol (40% by weight) on " Celite," was 2 metres in length and was kept at 70°. The carrier gas was nitrogen and the flow rate 0·8 (±0·05) l./hr. Liquid samples (0·005—0·1 ml., depending on their nature) were injected by means of an " Agla " micrometer syringe. The " elution time " of a compound, which we determined, was the interval (min.) between the origin of the chart record and the appropriate " peak."

The apparatus was employed incidentally to detect water, ethanol, diethyl ether, benzene, carbon disulphide, diethyl xanthate (and some unidentified related compounds), and constituents of light petroleum.

Potentiometry.—Apparatus and procedure were as before.[1]

Preparation of Sodium Ethyl Xanthate.—Carbon disulphide (10 ml.) was added to a cooled, filtered solution of sodium ethoxide made from sodium (4 g.) and ethanol (125 ml.). After 5—10 min., addition of water (15 ml.) and then ether (2 l.) produced pale-green lath-shaped crystals of sodium ethyl xanthate dihydrate (Found: H_2O, 20·0. Calc. for $C_3H_9NaO_3S_2$: $2H_2O$, 20·0%). This product, which lost water easily, was filtered off, washed with ether, and then

[5] Hantzsch and Bucerius, *Ber.*, 1926, **59**, 793
[6] Lund and Bjerrum, *Ber.*, 1931, **64**, 210.
[7] Martin and Green, *Ind. Eng. Chem. Analyt.*, 1933, **5**, 114.

converted into the anhydrous salt (A) (yield, 15—18 g., 65—75%) by drying overnight in a vacuum (P_2O_5) at room temperature (Found: C, 25·3; H, 3·6; S, 44·3; Na, 15·9. Calc. for $C_3H_5OS_2Na$: C, 25·0; H, 3·5; S, 44·4; Na, 16·0%). This was a hygroscopic pale-green powder: it was stored over P_2O_5 *in vacuo*.

Salt (A) dissolved readily, and completely, in acetone or water to give clear, pale-green solutions. A fresh aqueous solution gave a yellow precipitate with cupric sulphate solution and a bulky white precipitate with thallous sulphate solution, but no precipitate with barium chloride solution; addition of lead acetate (or nitrate) solution produced a pale-yellow suspension which slowly deposited a white coagulum. Dried xanthate (10 g.) which did not comply with these tests could normally be purified [8] by dissolving it in acetone (100 ml.) and then filtering the solution through sintered glass (porosity 4): addition of water (5 ml.) and then ether (500 ml.) to the filtrate produced crystals which were converted into salt (A) by drying overnight in a vacuum (P_2O_5) at room temperature.

Reactions of Sodium Ethyl Xanthate in Aqueous and in Ethanolic Solution.—(a) *With chloramine-T.* (i) In water.[9] A solution of salt (A) (7·5 g.; 0·052 mole) in water (100 ml.) was added dropwise to a rapidly stirred, cooled (about 5°) solution of chloramine-T trihydrate (15 g.; 0·053 mole) in water (1 l.). Then the mixture was saturated with sodium chloride (35 g.) and set aside at room temperature for 1 hr.

Pale-green $(C_2H_5O{\cdot}CS)_2S_2$ (" ethyl dixanthogen ") was collected (5 g., 80%). The colourless alkaline filtrate contained toluene-*p*-sulphonamide, residual chloramine-T, carbonate ($0{\cdot}5 \times 10^{-2}$ mole) and thiosulphate, but no xanthate, ethyl dixanthogen, or sulphur.

(ii) In ethanol. Reaction as in (i), but in ethanol, gave a precipitate containing sodium chloride (about 0·04 mole), and traces of carbonate and thiosulphate, but no sulphide or sulphur.

The almost colourless alkaline supernatant liquor (which did not contain residual chloramine-T) was decanted into a flask and distilled on a boiling-water bath under reduced pressure until only a moist yellowish solid (about 18 g.) remained; a colourless distillate (D) was collected (about 1050 ml.).

The residue was extracted with cold water (250 ml.), leaving insoluble material (1·25 g.; mainly sulphur). The filtrate was alkaline; xanthate, ethyl dixanthogen, carbonate, chloride, and thiosulphate were detected, but not sulphide or sulphate. When the filtrate was heated with an excess of 5N-hydrochloric acid, carbon disulphide ($0{\cdot}9 \times 10^{-2}$ mole), carbon dioxide, and traces of carbonyl sulphide and hydrogen sulphide were liberated. On cooling, the residual acid solution yielded colourless crystals of toluene-*p*-sulphonamide (hydrochloride?).

The distillate D was divided into three equal portions which were investigated separately:

(1) D1 did not contain carbon disulphide, carbonyl sulphide, or hydrogen sulphide; saponification gave sodium carbonate and sulphide (slowly in the cold, rapidly on warming). In a quantitative experiment, an aliquot part was mixed with an excess of 0·1N-sodium hydroxide (phenolphthalein); an excess of 10% barium chloride solution was then added, and the mixture was heated under reflux until precipitation of barium carbonate ceased. Residual sodium hydroxide was determined titrimetrically; the amount of sulphide produced (weighed as lead sulphide) was found by adding the neutralized mixture to an excess of lead acetate–acetic acid reagent (warming to remove lead carbonate). The whole of fraction D1 required $3{\cdot}06 \times 10^{-3}$ mole of sodium hydroxide for complete saponification, and $0{\cdot}86 \times 10^{-3}$ mole of sodium sulphide was produced thereby: thus $1{\cdot}10 \times 10^{-3}$ mole of sodium carbonate was obtained.

Addition of ethanolic silver nitrate solution to D1 produced a copious yellow precipitate, identified as silver thionitrate,[10] which darkened and became black (rapidly when water was added): the black residue was silver sulphide (Found: Ag, 85·1; S, 13·0. Calc. for Ag_2S: Ag, 87·1; S, 12·9%). The amount of silver sulphide recoverable from the whole of D1 was $0{\cdot}87 \times 10^{-3}$ mole, which is almost exactly equivalent to the yield of sodium sulphide obtained by saponification (see above). The mother-liquor contained nitric acid ($1{\cdot}76 \times 10^{-3}$ mole, estimated titrimetrically) equivalent to the amount of silver sulphide collected. Finally, when the neutralized mother-liquor was treated with an excess of aqueous sodium chloride solution (AgCl removed) and then heated with sodium hydroxide solution, sodium carbonate was produced, but not sodium sulphide.

[8] Du Rietz, *Svensk Kem. Tidskr.*, 1957, **69**, 310.
[9] Cambron and Whitby, *Canad. J. Res.*, 1930, **2**, 144.
[10] Poleck and Thummel, *Ber.*, 1883, **16**, 2435; Fanto, *Monatsh.*, 1903, **24**, 477.

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These results suggested that distillate D contained a (volatile) thion compound, which was not carbon disulphide or carbonyl sulphide and was readily converted, by alkaline hydrolysis or by silver nitrate, into the corresponding carbonyl compound (cf. the conversion of thioureas into ureas).

(2) Fraction D2 (1 vol.) was mixed with water (3 vol.) and extracted with carbon tetrachloride (3 × 100 ml.). The extract (E2) was washed with water (3 × 100 ml.), dried ($CaCl_2$), and filtered.

Like D, extract E2 gave a yellow precipitate with ethanolic silver nitrate solution which was converted by water into silver sulphide: the potential yield of this from the whole of E2 was $0{\cdot}85 \times 10^{-2}$ mole, which is 98% of the estimated recovery of that compound from D1 (or D2).

The remainder of extract E2 was concentrated to about one-twentieth of its original volume by distillation through a fractionating column (height, 50 cm.; diam., 1·5 cm.) packed with Fenske helices. The residual solution (about 15 ml.) was divided into two equal parts (E2/A, E2/A′) and one half was retained. E2/A′ was shaken with an excess of saturated (4%) ethanolic silver nitrate solution (50 ml.): a small quantity of water was then added, and silver sulphide (about 1 g.) was filtered off. On addition of more water to the filtrate, separation occurred, and the carbon tetrachloride layer (E2/B) was collected. E2/B was washed several times with water, dried ($CaCl_2$), and filtered.

E2/A and E2/B were then investigated by gas–liquid chromatography. Each was found to be a binary mixture consisting mainly of carbon tetrachloride (elution time, 3·7 min.); neither of them contained ethanol (elution time, 45 min.). The second constituent of E2/B (elution time, 10·2 min.) was diethyl carbonate. The second constituent of E2/A (elution time, 12·5 min.) was not diethyl carbonate (from its chromatographic behaviour). Since it had evidently reacted with silver nitrate to produce diethyl carbonate and silver sulphide (E2/A′ ⟶ E2/B), we concluded that the unknown constituent of E2/A was probably diethyl thioncarbonate, which had been extracted from distillate D.

(3) Fraction D3 (1 vol.) was mixed with water (3 vol.) and extracted with light petroleum (b. p. 34—35°) (3 × 100 ml.). The extract (E3) was washed with water (3 × 100 ml.), dried ($CaCl_2$), and filtered.

Extract E3, like D and E2, gave a yellow precipitate with ethanolic silver nitrate; this was converted by water into silver sulphide, the potential yield of which from the whole of E3 was estimated as $0{\cdot}85 \times 10^{-2}$ mole, *i.e.*, the same as the recovery from E2 (see above).

The remainder of extract E3 was concentrated to about one-fiftieth of its original volume by distillation through the fractionating column previously described. The residual solution (about 5 ml.) was heated on a boiling-water bath under reduced pressure until no light petroleum appeared to remain: the residue (0·6—0·8 g.) was impure diethyl thioncarbonate (Found: C, 45·5; H, 7·44; S, 23·5; OEt, 61·6. Calc. for $C_5H_{10}O_2S$: C, 44·8; H, 7·46; S, 23·9; OEt, 67·2%); its b. p., determined by Siwoloboff's method,[11] was 159°/770 mm. (lit.[12,13] 161—162°) but its density (1·02 at 20°) was less than recorded (about 1·03). The equivalent weight of the oil, determined by saponification, was 43·5 [Calc. for $(C_2H_5O)_2CS$: 44·7]; the amount of sulphide so obtained (weighed as lead sulphide) corresponded to 21·6% of sulphur in the original material (a trace of mercaptan was released during saponification). A similar proportion of reactive sulphur (22·6%) was recovered as silver sulphide on treatment of the oil with ethanolic silver nitrate and water (a yellow precipitate was produced initially).

The impurities present (each in small proportion) in our product, as shown by gas–liquid chromatography, were two trace constituents of the light petroleum, diethyl carbonate, and an unidentified compound (*O*-ethyl *S*-ethyl thiocarbonate?). We removed diethyl carbonate by (small-scale) fractional distillation, but failed to obtain a specimen of diethyl thioncarbonate whose chromatogram showed no traces of the other impurities. (Other workers[14] have reported difficulty in isolating this ester.)

(b) *With silver nitrate.* (i) One equivalent of silver nitrate. Silver nitrate (6·80 g.; 0·04 mole) in water or ethanol (500 ml.) was added in 1 hr. to a stirred solution of salt (A) (5·75 g.; 0·04 mole) in the same solvent (100 ml.), giving a yellow precipitate appreciably soluble in ethanol but

[11] Siwoloboff, *Ber.*, 1886, **19**, 795.
[12] Debus, *Ann. Chem. Pharm.*, 1850, **75**, 121.
[13] Salomon, *J. prakt. Chem.*, 1873, **6**, 433.
[14] Purvis, Jones, and Tasker, *J.*, 1910, **97**, 2287.

not in water. Then the mixture was set aside for 3 hr. and stirred occasionally. The precipitate was filtered off, washed with water, ethanol, and ether, and dried overnight in a vacuum (P_2O_5) at room temperature. The mother-liquor was retained.

The reaction in water [15] gave silver ethyl xanthate (8·9 g.) (Found: OEt, 20·0; Ag, 46·9. Calc. for $C_3H_5AgOS_2$: OEt, 19·65; Ag, 47·2%) (0·039 mole, 97%), which (0·30 g.) with hot 5N-hydrochloric acid (30 ml.) afforded almost 100% of silver chloride and carbon disulphide, with traces of carbonyl sulphide and hydrogen sulphide.

The reaction in ethanol also gave silver ethyl xanthate (Found: OEt, 19·1; Ag, 47·0%) (8·9 g., 97%).

(ii) Two equivalents of silver nitrate. Silver nitrate (13·6 g., 0·08 mole) in water (500 ml.) or ethanol (500 ml.) was added in 1 hr. to a stirred solution of salt (A) (0·04 mole) in the same solvent (100 ml.). A yellow precipitate was produced at first but, when more than half of the silver nitrate solution had been added, the colour changed to brown and eventually became almost black. After 3 hr., the precipitate was filtered off, washed with water only, and dried overnight in a vacuum (P_2O_5) at room temperature. The mother-liquor and washings were retained.

Reaction in water gave a black, plastic, unstable solid of variable composition. Silver xanthate was sometimes present. The material always appeared to contain disilver *O*-ethyl hydrogen dithio-orthocarbonate, $H(EtO{\cdot}COS_2)Ag_2$, as illustrated by two independent sets of results: (1) The product consisted mainly of the disilver salt (Found: OEt, 12·9; Ag, 62·6. Calc. for $C_4H_6O_2S_2Ag_2$: OEt, 12·7; Ag, 61·0%) (13·1 g., 0·037 mole). A sample (0·49 g., $1{\cdot}4 \times 10^{-3}$ mole) in hot 5N-hydrochloric acid (30 ml.) gave silver chloride ($2{\cdot}75 \times 10^{-3}$ mole), carbon disulphide ($0{\cdot}17 \times 10^{-3}$ mole), carbonyl sulphide ($1{\cdot}2 \times 10^{-3}$ mole), and hydrogen sulphide ($0{\cdot}77 \times 10^{-3}$ mole) but no carbon dioxide. (2) The product (11 g.) consisted of the disilver salt and silver ethyl xanthate in equal molar proportion (Found: OEt, 15·4; Ag, 55·9. Calc.: OEt, 15·4; Ag, 55·6%).

In the reaction with ethanol the yield (about 12 g.) and the composition of the solid product were variable. Moreover, the amounts of silver chloride, carbon disulphide, and hydrogen sulphide liberated by hot 5N-hydrochloric acid were also variable. Probably silver ethyl xanthate, silver hydrogen sulphide, and silver sulphide are involved in this product. The mother-liquor contained nitric acid (about 0·04 mole), but not silver or xanthate. After it had been diluted with water, carbon tetrachloride extracted diethyl carbonate (~0·015 mole) from it.

(iii) Four equivalents of silver nitrate. Silver nitrate (27·2 g.; 0·16 mole) in water (500 ml.) or ethanol (1000 ml.) was added during 1 hr. to a rapidly-stirred solution of salt (A) (0·04 mole) in the same solvent (100 ml.). The procedure of (i) was followed thereafter.

An experiment with anhydrous ethanol and exclusion of atmospheric moisture gave similar results to " absolute " ethanol.

Reaction in water [4] gave a black solid, apparently trisilver *O*-ethyl dithio-orthocarbonate or a 1 : 1 mixture of silver ethyl monothiocarbonate and silver sulphide (Found: OEt, 10·0; Ag, 70·2. Calc. for $C_3H_5Ag_3O_2S_2$: OEt, 9·8; Ag, 70·3%) (18·5 g., $4{\cdot}0 \times 10^{-3}$ mole). Heating a sample (0·55 g., $1{\cdot}2 \times 10^{-3}$ mole) with 5N-hydrochloric acid (30 ml.) gave silver chloride ($3{\cdot}6 \times 10^{-3}$ mole), carbonyl sulphide ($1{\cdot}1 \times 10^{-3}$ mole), and hydrogen sulphide ($1{\cdot}2 \times 10^{-3}$ mole) but no carbon disulphide. The mother-liquor contained nitric acid ($7{\cdot}9 \times 10^{-3}$ mole) and silver ions ($3{\cdot}5 \times 10^{-3}$ mole), but not xanthate.

The reaction in ethanol gave 98% pure silver sulphide (Found: Ag, 85·7. Calc. for Ag_2S: Ag, 87·1%) (19 g., $7{\cdot}6 \times 10^{-3}$ mole). This (0·24 g.) with hot 5N-hydrochloric acid (30 ml.) gave silver chloride ($1{\cdot}84 \times 10^{-3}$ mole), hydrogen sulphide ($0{\cdot}90 \times 10^{-3}$ mole), and carbon disulphide ($0{\cdot}02 \times 10^{-3}$ mole) but no carbonyl sulphide. Evidently, the product contained about 2% of silver ethyl xanthate (Found: OEt, 0·45%). The mother-liquor contained nitric acid ($10{\cdot}5 \times 10^{-3}$ mole) and silver ions ($3{\cdot}2 \times 10^{-3}$ mole), but not xanthate. Carbon tetrachloride removed, as above, diethyl carbonate (0·04 mole), identified by gas chromatography.

(iv) When aqueous 0·1N-silver nitrate solution was added to a dilute solution of salt (A) in ethanol, a reproducible one-step potentiometric-titration curve was obtained, and the equivalence-point gave an accurate indication of the amount of xanthate present (Fig. 1). Results in solely aqueous solution were variable.

(c) *With sodium hydroxide and silver nitrate.* (i) Silver nitrate (13·6 g. g., 0·08 mole) in water

[15] Cf. Reyschler, *Bull. Soc. chim. belges*, 1928, **37**, 166.

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(500 ml.) was added in 1 hr. to a stirred solution of salt (A) (5·75 g., 0·04 mole) and sodium hydroxide (1·60 g., 0·04 mole) in water (100 ml.). The procedure of b(ii) was followed thereafter. The unstable dark-brown product appeared to be impure disilver *O*-ethyl hydrogen dithio-orthocarbonate (Found: OEt, 13·1; Ag, 62·9. Calc. for $C_3H_6O_2S_2Ag_2$: OEt, 12·7; Ag, 61·0%) (13·7 g., 0·039 mole), which (0·44 g., $1·25 \times 10^{-3}$ mole) was heated with 5N-hydrochloric acid (30 ml.) to give silver chloride ($2·46 \times 10^{-3}$ mole), carbon disulphide ($0·58 \times 10^{-3}$ mole), carbonyl sulphide ($0·59 \times 10^{-3}$ mole), and hydrogen sulphide ($0·67 \times 10^{-3}$ mole) but no carbon dioxide. Thus silver and sulphur ($CS_2 + COS + H_2S$) were recovered in equal atomic proportion as required.

(d) *With hydrogen ions.* (i) When salt (A), or a sufficiently concentrated aqueous solution of it, was treated with a concentrated mineral acid, a heavy pale yellow oil with a characteristic pungent smell was produced: this decomposed slowly at room temperature (rapidly on warming), and was presumed to be *O*-ethyl hydrogen xanthate, $C_2H_5O{\cdot}CS_2H$.

FIG. 1. *Titration of sodium ethyl xanthate* (0·144 g.) *in ethanol* (100 ml.) *with* 0·1N-*aqueous hydrochloric acid* (○) *and silver nitrate* (●).

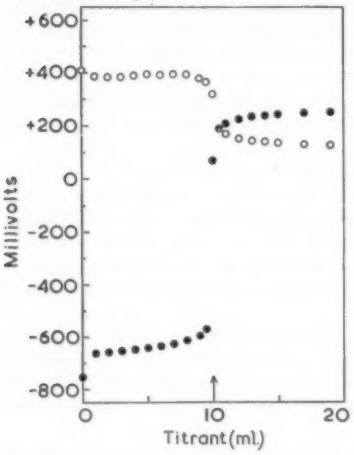
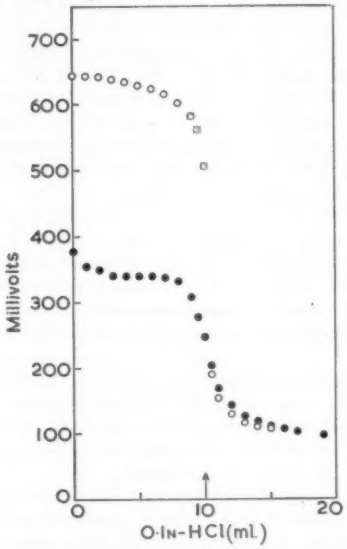


FIG. 2. *Titration of sodium hydroxide* (○) *and of sodium ethyl xanthate* (●) *in water with* 0·1N-*hydrochloric acid* (Sb *electrode*).



(ii) A fresh solution of salt (A) (0·11 g., $0·74 \times 10^{-3}$ mole) in water (50 ml.) was treated with 5N-hydrochloric acid (15 ml.): carbon disulphide ($0·74 \times 10^{-3}$ mole) was released, but not carbonyl sulphide, carbon dioxide, or hydrogen sulphide.

(iii) When the reaction between an aqueous solution of salt (A) (about 0·14 g./100 ml.) and 0·1N-hydrochloric acid was followed potentiometrically (antimony or glass electrode), the results varied with the method of titration. Only if the acid was added to the xanthate solution with intervals of several minutes between 0·5 ml. increments was the titration curve reproducible (Fig. 2).

Use of 0·1N-sulphuric acid always gave a one-step titration curve, although the curves for fast and slow titrations were usually different. Moreover, if thallous sulphate solution was added to the reaction mixture immediately after an excess of sulphuric acid had been introduced, thallous ethyl xanthate was precipitated, in substantial amount after a " fast " titration, but only in traces (or none) after a " slow " one.

Evidently, when sodium ethyl xanthate reacts with hydrogen ions in aqueous solution, ethyl xanthic acid persists for an appreciable period, even when its concentration is small, and hinders potentiometry. This difficulty did not arise when 0·1N hydrochloric or sulphuric acid was added, rapidly or slowly, to a solution of sodium xanthate in ethanol (Fig. 1).

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(iv) A solution of salt (A) (2·88 g.) in water (500 ml.) was prepared, and the xanthate concentration ($4·00 \times 10^{-2}$ mole/l.) was checked by titrating an aliquot part (50 ml.) with 0·1N-iodine.

Carbon dioxide was bubbled through a portion (50 ml.) for 30 min.: afterwards the concentration of xanthate was $3·86 \times 10^{-2}$ mole/l.

Hydrogen sulphide was bubbled through a portion (50 ml.) for 60 min., and then carbon dioxide was passed in for 30 min. in order to remove HS^- ions and hydrogen sulphide. The concentration of xanthate was then $3·81 \times 10^{-2}$ mole/l.

Evidently, unlike sodium trithiocarbonate,[1] sodium xanthate is decomposed only very slowly in aqueous solution by carbon dioxide or hydrogen sulphide.

(e) *With primary amines.* (i) Salt (A) (1·45 g., 0·01 mole), aniline (5 ml., 0·054 mole) and water (100 ml.) were heated in a sealed flask (air-space small) on a boiling-water bath for 3 hr., and then set aside at room temperature overnight. Colourless plates were collected and identified as *NN'*-diphenylthiourea (1·08 g., $0·47 \times 10^{-2}$ mole). The filtrate (containing hydrogen sulphide) was extracted with ether (2×50 ml.), in order to remove residual aniline and thiocarbanilide, and then evaporated, under reduced pressure, on a water-bath. The solid so obtained was extracted with acetone (50 ml.); sodium sulphide and carbonate were filtered off. Adding ether (500 ml.) to the acetone filtrate gave colourless needles of sodium phenyldithiocarbamate (0·51 g., $0·27 \times 10^{-2}$ mole).

(ii) In a similar experiment cyclohexylamine (5 ml.) gave *NN'*-dicyclohexylthiourea (Found: S, 12·7. Calc. for $C_{13}H_{24}N_2S$: S, 13·3%) (1·7 g., $0·70 \times 10^{-2}$ mole), m. p. 178°, sodium cyclohexyldithiocarbamate (0·35 g., $0·18 \times 10^{-2}$ mole), sodium sulphide, and carbonate.

Discussion

Ethanolysis of the $EtO{\cdot}CS_2^-$ *Ion.*—Di[alkoxy(thiocarbonyl)]disulphides, $(RO{\cdot}CS)_2S_2$, are readily prepared by oxidizing alkali-metal xanthates in aqueous solution with various reagents,[9,16] and we have obtained the diethyl compound (" ethyl dixanthogen ") in 80% yield by treating sodium ethyl xanthate, in water, with chloramine-T. However, this oxidation, in ethanol solution, gave very little ethyl dixanthogen and, instead, a 1 : 1 mixture of diethyl thioncarbonate, $(EtO)_2CS$, and sulphur; this reaction, which has not been observed before, is significant in the present context.

If sodium ethyl xanthate is oxidized in ethanol, and water is present (we used chloramine-T trihydrate and " absolute " alcohol), then, since ethyl dixanthogen is stable in ethanol containing chloroamine-T and so is not an intermediate, the new reaction must depend on ethanolysis of the xanthate ion, *i.e.*, reaction (2) (p. 117) followed by

$$HS^- + \left\{\begin{matrix} H_2O \\ EtOH \end{matrix}\right\} \rightleftharpoons \left\{\begin{matrix} HO^- \\ EtO^- \end{matrix}\right\} + H_2S$$

$$H_2S + O \xrightarrow{EtOH} H_2O + S$$

i.e., in sum, $$EtO{\cdot}CS_2^- + EtOH + RH + O \longrightarrow (EtO)_2CS + S + R^- + H_2O \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where R = HO or EtO.

This mechanism explains the salient experimental results, if we assume that about 80% of the available sodium ethyl xanthate was consumed in reaction (7), with most of the remainder unchanged. As regards the minor reaction products, the production of (*a*) thiosulphate and carbonate and (*b*) diethyl carbonate is consistent with the hydrolysis of small proportions of the xanthate and diethyl thioncarbonate, respectively, promoted by oxidation.

Equation (2) is also consistent with the diverse results we obtained by carefully adding silver nitrate in ethanol to ethanolic sodium ethyl xanthate. One equivalent (or less) of silver nitrate produced only silver ethyl xanthate and sodium nitrate:

$$EtO{\cdot}CS_2^- + Ag^+ \longrightarrow EtO{\cdot}CS_2Ag \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

But, if more than one equivalent was added, further reaction occurred until, with

[16] Zeise, *Schweitzer's Journal*, 1822, **36**, 36; *Berzelius Journal*, 1824, **3**, 82; 1837, **16**, 306.

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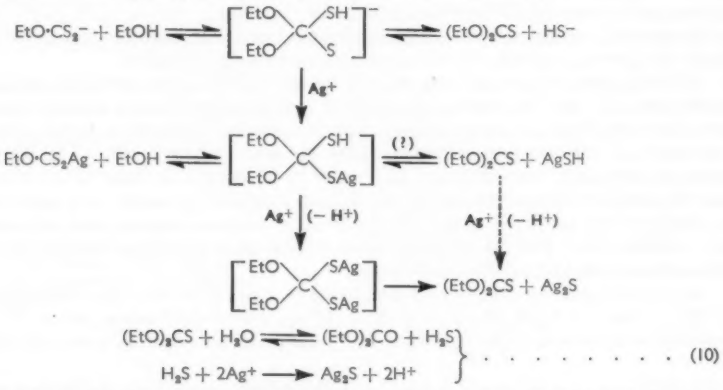
4 equivalents, diethyl carbonate, silver sulphide, nitric acid, and sodium nitrate were obtained in accordance with the reaction:

$$EtO{\cdot}CS_2^- + EtOH + H_2O + 4Ag^+ \longrightarrow (EtO)_2CO + 2Ag_2S + 3H^+ \quad . \quad . \quad . \quad . \quad . \quad (9)$$

A satisfactory mechanism for (9), which includes reaction (8), is based on the ethanolysis of the xanthate ion and the hydrolysis of diethyl thioncarbonate, namely:



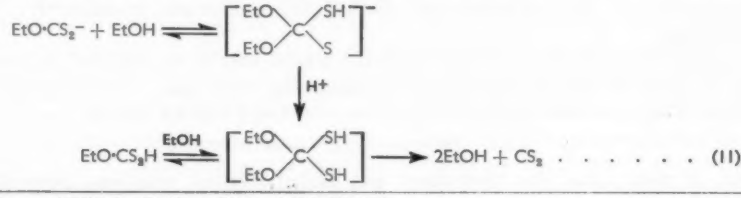
$$(EtO)_2CS + H_2O \rightleftharpoons (EtO)_2CO + H_2S$$
$$H_2S + 2Ag^+ \longrightarrow Ag_2S + 2H^+ \quad \Big\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

The inclusion of reactions (10) is justified by our observation that diethyl carbonate and silver sulphide were produced when diethyl thioncarbonate was treated with ethanolic silver nitrate in the presence of water. When reaction (9) was carried out in " absolute " alcohol (water-content about 0·5%), sufficient water for reaction (10) was still present; but, when reaction (9) occurred in anhydrous ethanol, the necessary water must have been produced from ethanol and nitric acid ($EtOH + HNO_3 \rightleftharpoons EtO{\cdot}NO_2 + H_2O$) and this would account for a relatively low yield of nitric acid in that experiment.

The mechanism proposed for reaction (9) also explains the results we obtained by adding two equivalents only of silver nitrate to sodium ethyl xanthate in ethanol, namely, production of diethyl carbonate and a mixture of silver ethyl xanthate and silver hydrogen sulphide and/or sulphide in variable proportions. Since diethyl thioncarbonate was *not* found we conclude that reaction (10) proceeded so quickly that there was insufficient silver nitrate to convert all the silver xanthate into diethyl thioncarbonate and silver hydrogen sulphide or sulphide. Evidently, reaction (9) cannot be stopped at the intermediate stage:

$$EtO{\cdot}CS_2^- + EtOH + 2Ag^+ \longrightarrow (EtO)_2CS + Ag_2S + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad (9a)$$

The foregoing proof of the addition of ethanol to the thiocarbonyl linkage of the xanthate ion revives an earlier suggestion [5] that the instability of ethyl hydrogen xanthate in the presence of ethanol might be due to the formation of an unstable addition product $(EtO)_2C(SH)_2$, which decomposes rapidly into carbon disulphide and ethanol. For if that hypothesis is combined with the present concept, plausible explanations of (*a*) the reaction between sodium ethyl xanthate and hydrogen ions in ethanol or ethanol–water and (*b*) the autocatalytic decomposition of ethyl hydrogen xanthate [17] are obtained:



[17] von Halban and Kirsch, *Z. phys. Chem.*, 1913, **82**, 325.

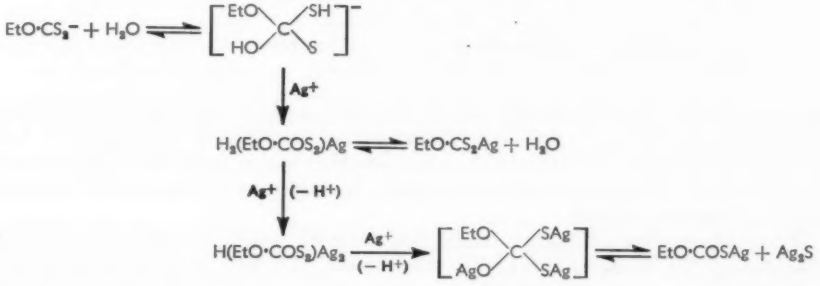
Hydrolysis of the $EtO{\cdot}CS_2^-$ *Ion.*—An analogous interpretation of the hydrolysis:

is consistent with the behaviour of sodium ethyl xanthate in water and in aqueous sodium hydroxide.

When up to one equivalent of silver nitrate is added gradually to aqueous sodium (or potassium [15]) ethyl xanthate, only silver ethyl xanthate is obtained, in accordance with reaction (8). If, however, more silver nitrate is then introduced, it reacts with the silver xanthate, causing the yellow precipitate to darken until, finally, it is black. Makens [4] decided that the end-product was a 1 : 1 mixture of silver ethyl monothiocarbonate and silver sulphide:

$$EtO{\cdot}CS_2Ag + H_2O + 2Ag^+ \longrightarrow EtO{\cdot}COSAg + Ag_2S + 2H^+ \quad . \; . \; . \; . \; (12)$$

Our analytical data also are consistent with this, but we think that the product, which is unique in both appearance and consistency, could well be trisilver *O*-ethyl dithio-orthocarbonate, $EtO{\cdot}COS_2Ag_3$, which decomposes (*e.g.*, when heated) into EtO·COSAg and Ag_2S. If so, a mechanism for reactions (8) and (12) can be formulated as follows:

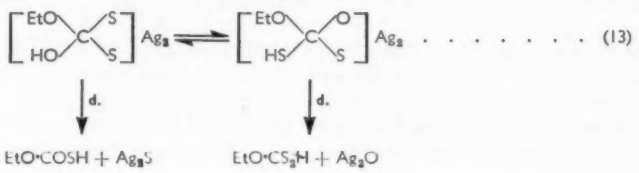


This scheme explains why pure silver xanthate is not obtained unless reaction (8) is carried out in a way which ensures that an excess of silver ions is avoided. It also suggests that reaction (12) might be stopped half-way:

$$EtO{\cdot}CS_2Ag + H_2O + Ag^+ \longrightarrow H(EtO{\cdot}COS_2)Ag_2 + H^+ \quad . \; . \; . \; . \; . \; . \; . \; (12a)$$

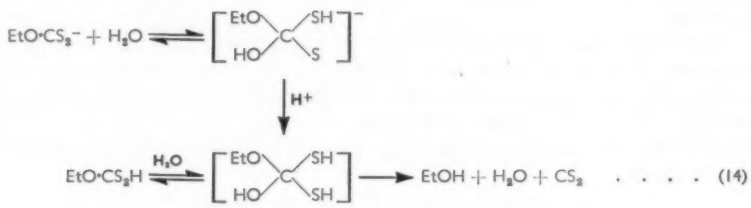
This can be achieved by treating sodium ethyl xanthate with exactly two equivalents of silver nitrate but, when the reaction occurs in water, there is a tendency for the disilver salt to be contaminated with silver xanthate; however, if one equivalent of sodium hydroxide is introduced as the reaction proceeds, hydrogen ions are removed continuously, and the salt $H(EtO{\cdot}COS_2)Ag_2$ is then obtained reproducibly.

Disilver hydrogen *O*-ethyl dithio-orthocarbonate decomposes at room temperature, yielding silver sulphide and oxide, carbonyl sulphide, and carbon disulphide; when heated with hydrochloric acid, it affords carbon disulphide, carbonyl sulphide, and hydrogen sulphide. This behaviour is consistent with isomerization:



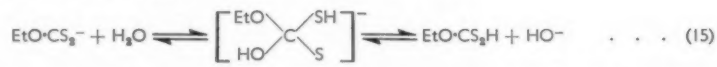
It is therefore interesting that we have isolated the disilver salt in two physical forms: a black plastic solid was obtained when reaction (12) occurred in water whereas, when sodium hydroxide was present, the product was a dark-brown powder.

Hydration of the xanthate ion also enables the reaction between sodium ethyl xanthate and hydrogen ions in water to be understood:



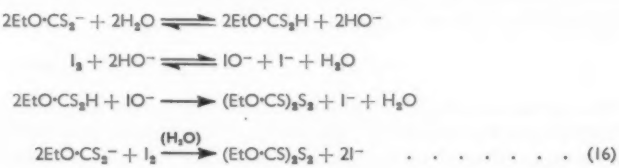
This mechanism, which follows the pattern of reactions (11), includes an unstable hydrate of ethyl hydrogen xanthate, as envisaged by Hantzsch and Bucerius,[5] in order to explain why that compound is stable when dry, yet decomposes rapidly in the presence of water.[17]

The production of xanthic acid from the hydrated xanthate ion can, however, be conceived in another way [see (4)]:

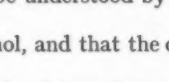


But although this alternative route affords a mechanism for the oxidation of the xanthate ion in water (see below), it does not explain its reaction with the hydrogen ion because (i) the complementary reaction $HO^- + H^+ \longrightarrow H_2O$ is not detected potentiometrically (Fig. 2), and (ii) the xanthate ion is not rapidly destroyed by carbon dioxide or hydrogen sulphide in aqueous solution.

When sodium ethyl xanthate is oxidized in water by means of chloramine-T or a soluble hypochlorite,[9] the oxidizing agent is presumably the ClO^- ion: thus, when iodine is used, the hypoiodite ion is very probably involved. But in order that IO^- ions should be available, the iodine must react with HO^- ions, and this can only be arranged in accordance with (16):



This mechanism explains the well-known iodometric estimation of xanthates in aqueous solution, for the amounts of iodine and xanthate consumed must be equivalent.

To sum up, it is now evident that the behaviour of sodium ethyl xanthate in both water and ethanol can be understood by supposing that the thiocarbonyl linkage is able to add on water or ethanol, and that the ortho-ion  (where X = HO or EtO) so produced is capable of dissociating in different ways according to the nature of X and the environment. Since this hypothesis has already served to explain the behaviour of sodium trithiocarbonate in ethanol and in water,[1] it may also be applicable to other thiocarbonyl compounds and in cases where XH is not ethanol or water. It appears that this is indeed the case, for the reaction between sodium ethyl xanthate and a primary

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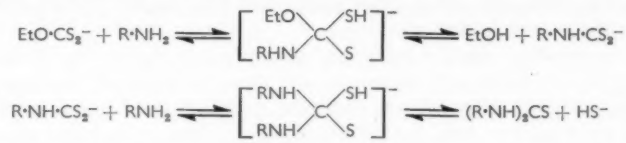
amine, which produces the corresponding sodium dithiocarbamate and *NN'*-disubstituted thiourea, can be formulated as follows:



We are grateful to D. A. Taylor for his assistance throughout this investigation, to Dr. C. A. Finch for advice on gas–liquid chromatography, and to M. Lonsdale for microanalyses.

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MAIDENHEAD, BERKS.

[*Received, June 9th,* 1960.]

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24. *Pteridine Studies. Part XIII.*[1] *Addition to 6-Hydroxypteridines.*

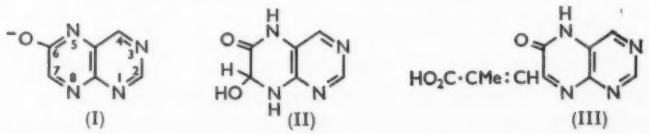
By ADRIEN ALBERT and FRIEDRICH REICH.

The methyl group in 6-hydroxy-7-methylpteridine had been found to hinder the characteristic addition of water across the 7,8-double bond of 6-hydroxypteridine. The electronic influences in such covalent hydrations are discussed, also why the 7,8-position is favoured and how the 7-methyl group opposes hydration. Similar influences are demonstrated in two natural products, xanthopterin and 7-methylxanthopterin.

Syntheses of six new hydroxy-methylpteridines are described. 6-Hydroxypteridine is shown to undergo Michael-like additions to the 7,8-double bond with ethyl malonate, ethyl cyanoacetate, and acetone.

6-HYDROXYPTERIDINE was the first heterocyclic substance recognized as undergoing reversible covalent hydration. The anion of 6-hydroxypteridine (I) is normal in that the ultraviolet spectrum agrees closely [2] with that of the neutral molecule of 6-aminopteridine, as is widely observed in aromatic chemistry; [3] also the sodium salt is anhydrous.[4]

The neutral molecule, however, rapidly undergoes (reversible) covalent hydration,[4] evidence for which is (*a*) the hysteresis loop traced during titration and back-titration [2] (p*K* 9·8 for the hydrated and 6·5 for the anhydrous form), (*b*) the long-wavelength ultraviolet absorption peak which is 67 mμ lower than that of the anion,[2] suggesting loss of a



(I) (II) (III)

double bond, (*c*) proof that neither ring-opening nor a 6,7-keto–enol shift occurred,[5] (*d*) identity of the ultraviolet spectra of the neutral molecule with that of 7,8-dihydro-6-hydroxypteridine,[6] and (*e*) the ease with which oxidation to 6,7-dihydroxypteridine can be effected.[6] It is therefore the 7,8-hydrate (II). The cation of 6-hydroxypteridine was shown to be hydrated in the same position.[6]

[1] Part XII, Brown and Jacobsen, *J.*, 1960, 1978.
[2] Albert, Brown, and Cheeseman, *J.*, 1952, 1620.
[3] Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2127.
[4] Albert, *J.*, 1955, 2690.
[5] Albert, "Ciba Symposium on the Chemistry and Biology of Pteridines," Churchill, London, 1954, p. 210.
[6] Brown and Mason, *J.*, 1956, 3443.

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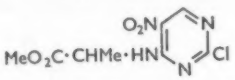
To test our hypothesis, that a 7-methyl group could sterically hinder covalent hydration, the synthesis of 6-hydroxy-7-methylpteridine was attempted. It was decided also to try to add, across the 7,8-double bond, weak acids other than water, particularly those commonly used in Michael condensations.

4,5-Diaminopyrimidine readily condenses with ethyl glyoxylate (or its hemiacetal), to give exclusively 6- or 7-hydroxypteridine in cold 2N-sulphuric acid [4] or boiling 2N-sodium carbonate [7] respectively. Hence it was surprising to find that 4,5-diaminopyrimidine gave no pteridine with ethyl pyruvate (or its acetal, or the free acid) under these conditions. Boiling 2N-sulphuric acid was also ineffective although it gives a 76% yield of 2-amino-4,6-dihydroxy-7-methyl- and 92% of 2,4-diamino-6-hydroxy-7-methyl-pteridine from pyruvic acid and the appropriate 4,5-diaminopyrimidine.[8] However, condensation in cold 5N-sulphuric acid gave us a 21% yield of the required 6-hydroxy-7-methylpteridine. This yield was increased to 60% in 5N-hydrochloric acid, the reaction being accelerated by the insolubility of the product.

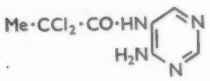
The reluctance of pyruvic acid to add electrophilically to 4,5-diaminopyrimidine is seen as the sum of two unfavourable inductive effects, the ester and the 5-amino-groups being insufficiently electron-attracting and -repelling respectively. Attempted condensation in 30N-sulphuric acid gave 7-(2-carboxyprop-1-enyl)-6-hydroxypteridine (III), which arose from dimerized pyruvic acid (other carboxypropenylpteridines have been isolated from pyruvic acid condensations [9]).

The identity of the 6-hydroxy-7-methylpteridine was confirmed by reduction to 7,8-dihydro-6-hydroxy-7-methylpteridine which was unambiguously synthesized as follows. 2,4-Dichloro-5-nitropyrimidine with alanine methyl ester gave methyl α-(2-chloro-5-nitro-4-pyrimidinylamino)propionate (IV); the nitro-group was then reduced, the ring closed, and the chlorine replaced by hydrogen. Surprisingly this dihydro-compound could not be used for preparing 6-hydroxy-7-methylpteridine as it resisted dehydrogenation and was destroyed on attempted oxidation owing largely to the liability of a 7-methyl group in pteridine.[10]

Attempts to prepare 6-hydroxy-7-methylpteridine by the cyclization of 4-amino-5-αα-dichloropropionamidopyrimidine (V) produced only trivial yields. Thus repeated evaporation of an aqueous solution, found suitable for a dichloroacetamido-analogue,[11] left the amide (V) unchanged, whereas the substance was destroyed when its silver derivative was refluxed with aqueous silver carbonate.[12] The amide (V), together with a little 4,5-bis-αα-dichloropropionamidopyrimidine, was readily formed from αα-dichloropropionyl chloride and 4,5-diaminopyrimidine.



(IV)



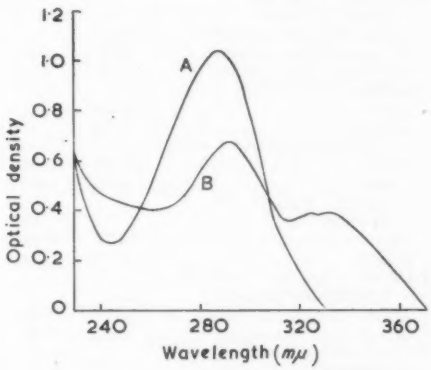
(V)

Two other attempts to prepare 6-hydroxy-7-methylpteridine were unsuccessful. When 4,5-diaminopyrimidine was condensed with ethyl ethoxalylacetate under acid conditions from pH 3·5 to −1, only 6-ethoxycarbonylmethyl-7-hydroxypteridine was produced, and this gave 7-hydroxy-6-methylpteridine (see p. 132) on hydrolysis and decarboxylation.[13] Again, 4,5-diaminopyrimidine and ethyl 2,4-dioxopentanoate in 10N-sulphuric acid gave mainly (and at pH 5, entirely) 6-acetonyl-7-hydroxypteridine which was degraded to 7-hydroxy-6-methylpteridine.

[7] Albert, Lister, and Pedersen, *J.*, 1956, 4621.
[8] Elion, Hitchings, and Russell, *J. Amer. Chem. Soc.*, 1950, **72**, 78.
[9] Pfleiderer, *Chem. Ber.*, 1956, **89**, 641; Russell, Purrmann, Schmitt, and Hitchings, *J. Amer. Chem. Soc.*, 1949, **71**, 3412.
[10] Albert, Brown, and Wood, *J.*, 1954, 3832.
[11] Sachs and Meyerheim, *Ber.*, 1908, **41**, 3957.
[12] Purrmann, *Annalen*, 1940, **546**, 98.
[13] Albert and Brown, *J.*, 1953, 74.

Properties of 6-Hydroxy-7-methylpteridine.—The neutral molecule was anhydrous when dried at 60°. A monosodium derivative, formed in N-sodium hydroxide, was anhydrous at 20°. Potentiometric titration of the anion differed from that of 6-hydroxypteridine in that no rapid drift of potential was encountered. The acid ionization (pK 7·17) corresponds to the anhydrous forms of 6-hydroxypteridine (see Table 1).

Whereas the stable neutral molecule of 6-hydroxypteridine has (at equilibrium) about 100 hydrated molecules to each anhydrous one,[6] the height of the 292 mμ peak for the equilibrated solution of the neutral molecule of 6-hydroxy-7-methylpteridine suggests that this is hydrated in a ratio of about 1 : 1 (see Figure, curve B). In addition there is a new peak of longer wavelength, evidence of extra conjugation. Further this peak, only 18 mμ below that of its anion, now lies within the normal range. Thus the hypothesis that a 7-methyl group would hinder the covalent hydration of 6-hydroxypteridine is substantiated. A less stable (hydrated) form of the neutral molecule of 6-hydroxy-7-methylpteridine, with a spectrum almost identical with that of the stable (hydrated) form of 6-hydroxypteridine, can be demonstrated spectroscopically (see Figure) by quickly



Ultraviolet spectra (in 1 cm. cells) of 6-hydroxy-7-methylpteridine (neutral molecules, 10⁻⁴M). (A) Hydrated form [solution of hydrated cation in 0·02N-hydrochloric acid adjusted to pH 6 (buffer) and measured at once]. (B) Equilibrium mixture of hydrated and anhydrous forms.

adjusting a 10^{-4}M-solution of the anhydrous form in 0·02N-hydrochloric acid to pH 6. It was stable for about 5 minutes (less stable at pH 7). This experiment also confirms the view that the cation of 6-hydroxy-7-methylpteridine is mainly in the hydrated form. The spectrum of the cation (see Table 1) does not change between 3 minutes (the time taken for dissolution and measurement) and 24 hours. Its spectrum and pK are almost identical with those of the cation of 6-hydroxypteridine; that these two pK's (3·7) are those of hydrates is seen by comparing them with those of 4- and 7-hydroxypteridine (−0·17 and 1·2 respectively [6]) which are not hydrated. The extra basic strength of the hydrates comes from the 4-aminopyridine type [14] of base-strengthening resonance (VI).

A 0·5N-solution of 6-hydroxy-7-methylpteridine in N-sulphuric acid was stable for at least 2 days at 20°, but a new substance (substance H) was formed when this solution was heated at 98° for 30 min. Analysis indicated that this was a hydrate of 6-hydroxy-7-methylpteridine. The substances have different R_F values (Table 2); also the spectrum in alkaline solution is not quite identical with that of 6-hydroxy-7-methylpteridine but slowly reverts to it. Cryoscopic measurements in N-sulphuric acid indicate that substance H is monomeric (Dr. D. D. Perrin, personal communication); it may be the 3,4-hydrate.

6-Hydroxy-7-methylpteridine gives substance H and two apparently dimeric by-products (one orange and one colourless) when boiled with water for 10 minutes. Whereas 6-hydroxypteridine is disproportionated by boiling N-sodium hydroxide, 6-hydroxy-7-methylpteridine is unaffected. The latter slowly dissolves in boiling methanol, giving a

[14] Albert, Goldacre, and Phillips, *J.*, 1948, 2240.

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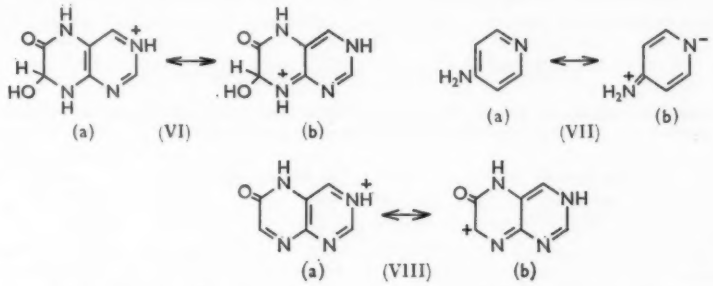
TABLE 1. *Physical properties of pteridines.*

	Ionization (H_2O; 20°) [a]			Spectroscopy in water [i]		
Pteridine	pK_a	spread (±)	concn.[b] (M)	$\lambda_{max.}$ (mμ)	log ε	pH
6-Hydroxy (hydrate, stable) ...	—	—	—	289 [f]	4·00	5·2
anion (anhydr., stable)	6·5 [c]	0·1	0·002	224, 256, 356 [f]	4·29, 3·97, 3·84	13·0
cation (hydrate, stable)	3·67 [d]	—	—	287 [d]	4·09	1·7
6-Hydroxy-7-methyl						
(hydrate, unstable)	—	—	—	288	4·02	6·0
(anhydr., stable)	—	—	—	292, 325 + 331	3·83, 3·58 + 3·58	5·5
anion (anhydr., stable)	7·17	0·03	0·007	225, 257, 349	4·43, 3·91, 3·96	12·0
cation (hydrate, stable)	3·72	0·05	0·007	288	4·09	1·0
6-Hydroxy-2-methyl						
(hydrate, stable)	—	—	—	*267*, 290	*3·90*, 4·04	6·5
anion (hydrate, unstable) ...	9·5 [c]	— [c]	0·004	—	—	—
anion (anhydr., stable)	6·31	0·02	0·004	222, 254, 364	4·40, 4·04, 3·86	12·1
cation (hydrate, stable)	4·67	0·04	0·004	285	4·09	2·0
6-Hydroxy-4-methyl						
(hydrate, stable)	—	—	—	285	4·02	5·25
anion (hydrate, unstable).....	9·5 [c]	— [c]	0·001	—	—	—
anion (anhydr., stable)	6·40	0·04	0·001	223, 259, 359	4·29, 3·94, 3·84	12·0
cation (hydrate, stable)	4·09	0·05	0·001	288	4·13	2·0
7,8-Dihydro-6-hydroxy.....	—	—	—	293 [d]	3·93	7·4
anion	10·54 [f]	—	—	305 [f]	4·07	13·0
cation	4·78	—	—	292 [d]	4·01	2·4
7,8-Dihydro-6-hydroxy-7-methyl	—	—	—	209, 294	4·52, 3·95	7·0
anion	10·89	0·05	0·002	223, 306	4·20, 4·06	13·0
cation	4·80	0·04	0·002	210, 292	4·37, 4·04	1·8
7-Acetonyl-7,8-dihydro-6-hydroxy	—	—	—	298	3·98	7·5
anion	10·79	0·05	0·005	311	4·05	12·0
cation	4·73	0·01	0·005	210, 293	4·38, 4·04	1·0
7-Di(ethoxycarbonyl)methyl-7,8-dihydro-6-hydroxy	—	—	—	210, 293	4·48, 3·96	7·0
anion	10·17	0·05	0·005	—	—	—
cation	4·12	0·04	0·003	210, 292	4·32, 4·02	1·0
7-Cyanomethyl-7,8-dihydro-6-hydroxy	—	—	—	209, 293	4·48, 3·96	7·0
anion	9·89	0·06	0·003	214, 304	4·51, 4·08	12·0
cation	4·18	0·03	0·003	209, 291	4·42, 4·05	1·2
7-(2-Carboxyprop-1-enyl)-6-hydroxypteridine (III)						
anion	2·93 [g]	0·05	0·003	224, *255*, 383	4·28, *4·05*, 4·07	8·0
cation	5·69 [g]	0·04	0·003	287	4·14	0
7-Hydroxy	—	—	—	227, 248 + 256, 303 [d]	3·79, 3·44 + 3·45, 4·00	4·0
anion	6·41 [d]	—	—	226, 260, 326 [d]	4·27, 3·76, 4·04	9·0
cation	1·2 [d]	—	—	—	—	—
7-Hydroxy-6-methyl	—	—	—	257, 299	3·54, 4·09	4·7
anion	6·97	0·03	0·02	*225*, 261, 324	*4·19*, 3·66, 4·12	9·2
7-Hydroxy-2-methyl	—	—	—	*259*, 305	*3·52*, 4·09	4·5
anion	6·68	0·03	0·005	213, 258, 327	4·40, 3·69, 4·10	9·0
cation	1·71 [h]	0·04	0·01	210, 294	4·40, 4·04	−0·8
7-Hydroxy-4-methyl	—	—	—	253 + 260, 304	3·46 + 3·46, 4·00	4·0
anion	6·79	0·05	0·005	228, *256*, 327	4·37, *3·74*, 4·03	9·3
cation	<2	—	0·01	—	—	—

[a] Determined potentiometrically. [b] Where no figure appears in this column, the results have been quoted, from the literature, for comparison. [c] More accurate figures than previously published (see Experimental section). [d] Albert, Brown, and Cheeseman, *J.*, 1951, 1620. [e] Determined in a single potentiometric titration and, owing to concomitant dehydration, may be low by about 0·5. [f] Brown and Mason, *J.*, 1956, 3443. [g] No hysteresis detected. [h] Each reading, significantly different from values obtained by titrating water under the same conditions, was corrected for mean ionic activity (Davies, *J.*, 1938, 2093). [i] 1 and 4 cm. cells; shoulders in italics. [j] Decomposes at pH 12.

1 : 1 addition product which is rapidly reconverted into 6-hydroxy-7-methylpteridine in 0·1N-sodium hydroxide.



It is remarkable that 6-hydroxypteridine has so strong a tendency to hydration whereas 7-hydroxypteridine has none. The hydrated form of the cation of 6-hydroxypteridine appears to be stabilized mainly by the energy of the resonance hybrid (VI), referred to above, and the hydrated neutral molecule by a similar but smaller resonance of the type (VII) which is well known in the neutral molecule of 4-aminopyridine where it was demonstrated by dipole-moment measurements.[15] No other hydroxypteridines can gain these types of resonance stabilization by hydration. 6-Hydroxy-4-methylpteridine (Table 1) closely resembles 6-hydroxypteridine in having a highly stable hydrate as neutral molecule.

Next, it is necessary to consider how a 7-methyl group reduces the tendency of 6-hydroxypteridine to hydration. The known mechanism of the hydration of C:C links [16] indicates that position 7 in 6-hydroxypteridine should be positively charged to invite nucleophilic addition of a water molecule. However, this position in the neutral molecule is negatively charged both from the inductive effect of $N_{(8)}$ and the mesomeric influence of the carbonyl group. Thus the cation (VIII), particularly a mesomeric form (VIIIb), is the species most likely to undergo hydration. A 7-methyl group would exercise a small unfavourable inductive effect on hydration at position 7, but its main effect is to offer steric hindrance to the approach of the water molecule. Thus, the rate of dehydration (of neutral hydrated species at pH 8·6 and 20°) is comparable with that of 6-hydroxypteridine (Dr. D. D. Perrin, personal communication). Discrepancies in the literature concerning the reported water content of xanthopterin (2-amino-4,6-dihydroxypteridine) may have a similar origin. This substance was first reported as a hemihydrate,[17] then in an anhydrous form,[18] but later, in the same laboratory, xanthopterin could not be obtained with less water than the monohydrate.[19] Here also, the insertion of a 7-methyl group considerably lessens the tendency to hydration. We find that at pH 4, where both substances are present only as neutral molecules, the 378 mμ peak of 7-methylxanthopterin has exactly twice the height of the corresponding peak of equilibrated xanthopterin (385 mμ). This agrees with Schou's demonstration [20] that xanthopterin is, under these conditions, a mixture of equal amounts of two related substances: we believe that here the 385 mμ peak refers to the anhydrous form, and the 305 mμ shoulder to the 7,8-hydrate, and that 7-methylxanthopterin, which shows no equilibration phenomena, is substantially anhydrous.

Michael-type Additions.—Additions, other than of water, to the 7,8-double bond in 6-hydroxypteridine have been demonstrated for hydroxylamine, ammonia, a second

[15] Angyal and Angyal, *J.*, 1952, 1461.
[16] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 695.
[17] Purrmann, *Annalen*, 1941, **548**, 291.
[18] Korte, *Chem. Ber.*, 1954, **87**, 1062.
[19] Korte and Barkemeyer, *Chem. Ber.*, 1956, **89**, 2400.
[20] Schou, *Arch. Biochem.*, 1950, **28**, 10.

molecule of 6-hydroxypteridine, and 7,8-dihydro-6-hydroxypteridine.[4] This encouraged us to use the reagents active in Michael condensations, *e.g.*, ethyl malonate. The C:N group reacts with these in benzylideneaniline, but not in heteroaromatic nuclei (*e.g.*, pyridine) unless more pronounced electron-withdrawing influences are provided (as in nicotinamide

TABLE 2. *R_F values* (paper chromatography).

Substances were dissolved in cold 0·1N-sodium hydroxide, immediately before application to the paper (Whatman No. 1), which was rapidly transferred to the solvent jar.

Substance	In 3% aq. NH_4Cl		In butanol–5N-acetic acid (7 : 3)	
Picric acid (for comparison)	0·55	D	0·55	D
6-Hydroxy-7-methylpteridine	0·70	D [a]	0·60	V [a]
Substance H (p. 129)	0·50—0·60	D	0·30	D
7-Hydroxy-6-methylpteridine	0·70	D [b] ⟶ F	0·65	D [b] ⟶ F
7,8-Dihydro-6-hydroxy-7-methylpteridine	0·55	D	0·50	D
7-Carboxypropenyl-6-hydroxypteridine	0·85	D	0·70	D

The dried paper was read in ultraviolet light of (principally) 254 mμ. Interpretation: D, dark (absorption) spot. F, blue fluorescent spot. D ⟶ F, dark spot which changes to a blue fluorescence after irradiation for 1 min. V, violet absorption spot. [a] Same in light of 360 mμ. [b] Invisible in light of 360 mμ.

methochloride [21] or acridine [22]). Thus it appeared that Michael-like additions to the C:N bond are similar to the addition of water and should yield more stable products, in as much as acridine shows no tendency to add water.

We found that 6-hydroxypteridine, in cold alkaline solution, readily reacted with acetone, diethyl malonate, and ethyl cyanoacetate, the carbanion adding to $C_{(7)}$ and the mobile hydrogen to $N_{(8)}$. The acetone adduct was characterized as its semicarbazone, and the ethyl cyanoacetate adduct was degraded to 7-cyanomethyl-7,8-dihydro-6-hydroxypteridine. All the adducts gave 6,7-dihydroxypteridine [2] when heated with N-sodium hydroxide (in air), thus establishing the orientation. The resemblance of the spectra and ionization constants of 7,8-dihydro-6-hydroxypteridine and these adducts is noteworthy (Table 1).

7-Hydroxy- and 6-hydroxy-7-methyl-pteridine did not react with acetone under these conditions, and 6-hydroxypteridine did not react at pH 2 or in acetone alone.

7-Hydroxypteridines.—Contrary to expectation, very little 7-hydroxy-6-methylpteridine was formed from ethyl pyruvate and 4,5-diaminopyrimidine in water in the range pH 5·5—14 * between 20° and 100°. However, in cold aqueous solution (at pH 4) these substances slowly gave the required pteridine. The new isomer was distinguished from 6-hydroxy-7-methylpteridine by the fluorescence after photoreduction [23] on paper (Table 2). Its orientation was confirmed by methylation to the known, sharply melting, 5,6-dihydro-6,8-dimethyl-7-oxopteridine.[24] It was easily converted into 7-chloro-6-methylpteridine, but resisted reduction with potassium borohydride.

7-Hydroxy-2(and 4)-methylpteridine were prepared without difficulty from ethyl glyoxylate hemiacetal and 2- and 6-methyl-4,5-diaminopyrimidine respectively in 2N-sodium carbonate.

EXPERIMENTAL

Elementary analyses were carried out by the Analytical Section of this Department, under Dr. J. E. Fildes. Yields are based on the stage in purification when the substances first gave a single spot in paper chromatography, but further purification was carried out before analysis.

* Between pH 1 and 3, neither 6-hydroxy-7- nor 7-hydroxy-6-methylpteridine could be isolated, but a small amount of a new substance with a double spot in paper chromatography.

[21] Eys and Kaplan, *J. Biol. Chem.*, 1957, **228**, 305.
[22] Kröhnke and Honig, *Annalen*, 1959, **624**, 97.
[23] Albert, *Nature*, 1956, **178**, 1072.
[24] Albert, Brown, and Wood, *J.*, 1956, 2066.

Ultraviolet spectra were measured on a Perkin–Elmer "Spectrocord" recording spectrophotometer, and the $\lambda_{max.}$ and extinction values rechecked on a Hilger "Uvispek" manual instrument (1 cm. cells). Ionization constants were determined as in earlier work from this Department.

Acid Ionization Constant of 6-Hydroxypteridine.—Five portions (each 0·04150 g.) were separately dissolved in boiled-out water (125 ml.). Each was titrated with two successive portions of 0·1N-potassium hydroxide (each portion: 0·1 equiv.). This allowed the upper curve of the hysteresis loop [2] to be traced more accurately than before (see Table 1).

6-Hydroxy-7-methylpteridine.—4,5-Diaminopyrimidine [25] (2·2 g., 0·02 mole) was suspended in water (10 ml.) and dissolved by the dropwise addition of 10N-hydrochloric acid. Ethyl pyruvate [26] (3·4 g., 1·5 equiv.) and 10N-hydrochloric acid (10 ml. altogether) were added, quickly, in that order and the mixture was shaken for 6 hr. at about 20°, then refrigerated overnight and filtered. The precipitated *hydrochloride* was washed with N-hydrochloric acid and filtered off (Found, for a sample washed with alcohol and dried at 20°: Cl, 21·2; N, 26·9. $C_7H_8N_4O,1{\cdot}25HCl$ requires Cl, 21·3; N, 26·95%). The mixed hydrochlorides were shaken for an hour in M-sodium citrate (20 ml.), being adjusted to pH 5, if necessary, after the first ½ hr. The suspension was refrigerated, filtered, and washed free from chloride, giving 60% of colourless 6-hydroxy-7-methylpteridine, which was purified, as the *sodium salt*, by dissolution of 0·9 g. in 10N-sodium hydroxide (1 ml.) and boiled-out water (9 ml.). The yellow crystals were washed with N-sodium hydroxide, then with alcohol and dried at 20°/0·01 mm. over P_2O_5 (Found: C, 45·2; H, 2·9; N, 30·2. $C_7H_5N_4NaO$ requires C, 45·05; H, 2·7; N, 30·4%). The aqueous solution, adjusted to pH 5, gave pure *6-hydroxy-7-methylpteridine* (Found, for material dried at 60°/0·01 mm.: C, 51·4; H, 4·1; N, 34·2. $C_7H_6N_4O$ requires C, 51·85; H, 3·7; N, 34·6%). Drying in air at 100° produces an intense orange colour.

This substance (0·1 g.) was boiled with methanol (50 ml.) for 10 min. The mixture was filtered and concentrated to 2 ml., giving *7,8-dihydro-6-hydroxy-7-methoxy-7-methylpteridine* (60%) (Found, for material dried at 20°: C, 49·3; H, 5·55; N, 29·5. $C_8H_{10}N_4O_2$ requires C, 49·5; H, 5·2; N, 28·9%). It readily decomposes to 6-hydroxy-7-methylpteridine in cold, dilute alkali.

7-(2-Carboxyprop-1-enyl)-6-hydroxypteridine (III).—4,5-Diaminopyrimidine (1·1 g.), ethyl pyruvate (2·2 g.), and 30N-sulphuric acid (4 ml., 10 equiv.) were set aside at 20° for a week, then adjusted to pH 4 with sodium hydroxide. The colourless *7-(2-carboxyprop-1-enyl)-6-hydroxypteridine* (27%) was filtered off and recrystallized from 200 parts of boiling water. It gives the iodoform test, decolorizes bromine water, and chars at 240° (Found, for material dried at 20°: C, 51·9; H, 3·55; N, 24·4. $C_{10}H_8N_4O_3$ requires C, 51·7; H, 3·5; N, 24·1%).

7,8-Dihydro-6-hydroxy-7-methylpteridine.—(a) *By the reduction of 6-hydroxy-7-methylpteridine.* Anhydrous 6-hydroxy-7-methylpteridine (0·16 g.), 0·1N-sodium hydroxide (11 ml.), and potassium borohydride (0·027 g.), set aside at 20° for 11 hr. and then brought to pH 7 with phosphoric acid gave a precipitate (90%) of 7,8-dihydro-6-hydroxy-7-methylpteridine. This was recrystallized from 200 parts of water and found by infrared and ultraviolet spectroscopy to be identical with the substance synthesized as below.

(b) *Direct synthesis.* Alanine methyl ester (5 g.) was added at 0° to a stirred solution of 2,4-dichloro-5-nitropyrimidine [25] (5 g.) in ether emulsified in a suspension of sodium hydrogen carbonate (8 g.) in water (25 ml.). Stirring was continued for 30 min. at 0° and 15 min. at 20°. The precipitate was filtered off, dried, and recrystallized from light petroleum (b. p. 100—120°), giving *methyl α-(2′-chloro-5′-nitro-4′-pyrimidinylamino)propionate* (IV), m. p. 105° (88%) (Found: C, 36·8; H, 3·55; Cl, 13·65. $C_8H_9ClN_4O_4$ requires C, 36·8; H, 3·5; Cl, 13·6%). This ester (5 g.) in methanol (350 ml.) was hydrogenated at room temperature and pressure over Raney nickel and calcium carbonate. After the nitro-group had been reduced, the mixture was filtered and refluxed with water (20 ml.) for 30 min. to effect ring-closure. Water (150 ml.) was added, and the mixture concentrated to 200 ml., and later to 50 ml., giving two crops (total 80%) of *2-chloro-7,8-dihydro-6-hydroxy-7-methylpteridine*, decomp. about 260° (Found: C, 42·2; H, 3·6; N, 28·05. $C_7H_7ClN_4O$ requires C, 42·3; H, 3·55; N, 28·2%). This substance (1 g.), red phosphorus (1 g.), and hydriodic acid (6 ml.; *d* 1·7) were heated at 160° for 1 hr. Water (3 ml.) was added, and the filtrate adjusted to pH 7·5 with "Tris" buffer, giving

[25] Brown, *J. Appl. Chem.*, 1952, **2**, 239.
[26] Böeseken and Felix, *Ber.*, 1929, **62**, 1315.

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7,8-*dihydro*-6-*hydroxy*-7-*methylpteridine* (85%), which recrystallized from 200 parts of water (Found: C, 51·3; H, 5·1; N, 33·4. $C_7H_8N_4O$ requires C, 51·2; H, 5·0; N, 34·1%). It has a sparingly soluble potassium salt.

4-*Amino*-5-αα-*dichloropropionamidopyrimidine* (V).—αα-Dichloropropionyl chloride [27] (2·9 g.) was added to a stirred solution of 4,5-diaminopyrimidine (1·1 g., 0·5 equiv.) in dried pyridine (70 ml.) at 100°. After 30 min. at 100°, the pyridine was recovered and water (10 ml.) was added to the warm residue. The solid which was deposited on cooling recrystallized from 50 parts of light petroleum (b. p. 60—70°), giving 0·1 g. of 4,5-*bis*-αα-*dichloropropionamidopyrimidine*, m. p. 137—139° (Found: C, 33·2; H, 2·8; N, 15·7; Cl, 39·5. $C_{10}H_{10}Cl_4N_4O_2$ requires C, 33·4; H, 2·8; N, 15·6; Cl, 39·4%). It is insoluble in N-acetic or boiling 0·1N-hydrochloric acid, hence it is not the 5,5-diacyl isomer which would be highly basic.

The filtrate (pH 3) from the diacyl derivative was adjusted to pH 7 with 3N-sodium hydroxide (about 8 ml.). The solid deposited was recrystallized from 30 parts of water, and then 120 parts of benzene, giving 4-*amino*-5-αα-*dichloropropionamidopyrimidine* (0·8 g.), m. p. 144° (slight decomp.), soluble in cold N-acetic acid (Found: C, 35·7; H, 3·5; N, 23·8. $C_7H_8Cl_2N_4O$ requires C, 35·8; H, 3·4; N, 23·8%). It was unchanged by sodium iodide in refluxing acetone.

Substance H (see p. 129).—6-Hydroxy-7-methylpteridine (0·5 g.) and N-sulphuric acid (6 ml., 2 equiv.) were heated at 98° in a sealed tube for 30 min. and cooled. N-Sodium citrate was added, then enough N-sodium hydroxide to give pH 5·5. The precipitate was shaken with 20-ml. portions of cold water until chloride-free, and then with cold water (500 ml.) for an hour, filtered, and concentrated to 25 ml. below 40°. The pale crystals of *substance H* are soluble in 1200 parts of cold water (Found, for material dried at 20°: C, 46·8; H, 4·7; N, 30·5. $C_7H_8N_4O_2$ requires C, 46·7; H, 4·5; N, 31·1%).

6-*Hydroxy*-2- *and* -4-*methylpteridine*.—4,5-Diamino-2-methylpyrimidine [10] (1·24 g., 0·01 mole), ethyl glyoxylate hemiacetal (2 g.), and 2N-sulphuric acid (18 ml.) were set aside for 5 days at 37°, then brought to pH 6 with sodium citrate (1 g.) and 10N-sodium hydroxide. The precipitate of 6-*hydroxy*-2-*methylpteridine* when recrystallized from water (130 parts; 85% yield) began to char above 200° (Found, for material dried at 160°/0·01 mm.: C, 46·6; H, 4·8; N, 30·9. $C_7H_6N_4O,H_2O$ requires C, 46·7; H, 4·5; N, 31·1%).

6-*Hydroxy*-4-*methylpteridine* was similarly obtained from 4,5-diamino-6-methylpyrimidine [10] in 75% yield. It becomes brown at about 230° (Found, for material dried at 160°/0·01 mm.: C, 47·2; H, 4·4; N, 31·1%). Both isomers give a very elongated spot, similar to that of 6-hydroxypteridine on paper chromatography in butanol–acetic acid. None of the 7-hydroxy-isomers (see below) was formed in these reactions.

6-*Hydroxypteridine and Acetone*.—6-Hydroxypteridine hydrate (0·66 g., 0·004 mole), 0·1N-sodium hydroxide (80 ml.), and acetone (10 ml., 40 equiv.) were left at 20° for 2 days. The solution was adjusted to pH 6 (sodium citrate + 5N-sulphuric acid), concentrated to 40 ml. (charcoal), and chilled. The product, recrystallized from 60 parts of water, gave 80% of 7-*acetonyl*-7,8-*dihydro*-6-*hydroxypteridine*, decomp. about 250° (Found: C, 52·2; H, 4·9; N, 26·6. $C_9H_{10}N_4O_2$ requires C, 52·4; H, 4·9; N, 27·2%). This gave a positive iodoform test, and was unchanged by refluxing with an excess of 5N-hydrochloric acid for 6 hr., but boiling N-sodium hydroxide (1 hr.) produced 50% of 6,7-dihydroxypteridine by oxidative hydrolysis. The acetonyl compound resisted oxidation by boiling ferric chloride solution, by hot air at 110° (60 hr.), and by potassium dichromate in boiling N-sulphuric acid. Cold alkaline potassium permanganate solution caused gross destruction. The *semicarbazone* (90% yield) formed colourless crystals from 350 parts of water, decomp. 235° (Found: C, 45·2; H, 5·25. $C_{10}H_{13}N_7O_2$ requires C, 45·6; H, 5·0%).

6-*Hydroxypteridine and Ethyl Malonate*.—6-Hydroxypteridine hydrate (1·66 g.), in hot N-sodium carbonate (30 ml.), was shaken with ethyl malonate (6·4 g.) at 20° for 15 hr. The separated solid was recrystallized from 80 parts of water, giving 60% of 7-*diethoxycarbonylmethyl*-7,8-*dihydro*-6-*hydroxypteridine*, m. p. 184—188° (decomp.) (Found: C, 50·6; H, 5·2; N, 18·3. $C_{13}H_{16}N_4O_5$ requires C, 50·6; H, 5·2; N, 18·2%). This gave a *picrate*, m. p. 217—219° (from water) (Found: C, 42·85; H, 3·45; N, 18·25. $C_{19}H_{19}N_7O_{12}$ requires C, 42·5; H, 3·6; N, 18·25%). Refluxing in 0·1N-hydrochloric acid for 5 hr. produced no change. Attempted dehydrogenations with potassium permanganate, ferric chloride, and boiling nitrobenzene were unsuccessful.

[27] Leimer, *Ber.*, 1937, **70**, 1050.

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6-Hydroxypteridine and Ethyl Cyanoacetate.—6-Hydroxypteridine hydrate (0·33 g., 0·002 mole), N-sodium hydroxide (6 ml.), and ethyl cyanoacetate (0·45 g., 2 equiv.) were set aside overnight at 20°, then brought to pH 7 with phosphoric acid. The crystals of the sodium salt of 7-(α-cyano-α-ethoxycarbonylmethyl)-7,8-dihydro-6-hydroxypteridine (R_F 0·65) were boiled with water (10 ml.) for 5 min., giving the sodium salt of 7-(α-cyano-α-carboxymethyl)-7,8-dihydro-6-hydroxypteridine (R_F 0·10), which was precipitated (as the free acid) at pH 2. This acid and water (5 ml.), refluxed for 2 hr., deposited colourless *7-cyanomethyl-7,8-dihydro-6-hydroxypteridine* (R_F 0·50; all R_F's refer to butanol–5N-acetic acid, 7 : 3) (yield, 77% based on 6-hydroxypteridine) (Found, for material dried at 20°: C, 50·8; H, 3·95; N, 36·9. $C_8H_7N_5O$ requires C, 50·8; H, 3·7; N, 37·0%).

7-Hydroxy-6-methylpteridine and its Methylation.—4,5-Diaminopyrimidine (3·3 g.), ethyl pyruvate (4 ml.), and water (75 ml.) were set aside at 20° for 4 days (final pH, 3·5—4). 10N-Sodium hydroxide (5 ml.) was added and the suspension boiled for 3 min. and adjusted to pH 5. The precipitate was extracted with boiling water (110 ml.), giving (on chilling) *7-hydroxy-6-methylpteridine* (50%), soluble in 35 parts of boiling water and in cold N-hydrochloric acid (Found: C, 51·95; H, 3·5; N, 34·6. $C_7H_6N_4O$ requires C, 51·85; H, 3·7; N, 34·6%). The sodium salt crystallized (90% recovery) from 2 equivalents of boiling N-sodium hydroxide. Methyl sulphate (0·12 ml., 1·2 equiv.) was shaken with 7-hydroxy-6-methylpteridine (0·16 g.) in N-potassium hydroxide (1 ml.) at 20° for 30 min. while the pH was kept at 8 by adding N-potassium hydroxide. Extraction with chloroform (4 + 3 ml.) gave 7,8-dihydro-6,8-dimethyl-7-oxopteridine (70%) (from benzene),[24] m. p. and mixed m. p. 146—147°.

7-Chloro-6-methylpteridine.—7-Hydroxy-6-methylpteridine (0·5 g.), phosphorus trichloride (25 ml.), and phosphorus pentachloride (2·5 g.) were refluxed for 6 hr. or until clear. The volatile materials were removed at 100 mm. The residual solid was powdered in a chilled mortar, and ice (10 g.) added in one portion. The slurry was adjusted to pH 7—8 with potassium carbonate, clarified, and extracted with twice its volume of chloroform. The lower layer was dried (Na_2SO_4) and the solvent removed below 40° to prevent dimerization. The product was extracted with cold benzene (5 ml.). The extract, on concentration, deposited *7-chloro-6-methylpteridine*, m. p. 103° (Found: C, 46·0; H, 2·7. $C_7H_5ClN_4$ requires C, 46·6; H, 2·8%). The yield, 50%, fell to 30% when 1 g. of the hydroxypteridine was used. Omission of phosphorus trichloride caused much charring.

7-Hydroxy-2(and 4)-methylpteridine.—4,5-Diamino-2-methylpyrimidine [10] (1·24 g.), 2N-sodium carbonate (10 ml.), and ethyl glyoxylate hemiacetal (2 g.) were refluxed vigorously for 1 hr., then cooled and adjusted to pH 5 with 5N-sulphuric acid. The precipitate recrystallized from 80 parts of water, giving *7-hydroxy-2-methylpteridine* (85%), m. p. 265° (decomp.) (Found: C, 52·0; H, 3·7; N, 34·6. $C_7H_6N_4O$ requires C, 51·85; H, 3·7; N, 34·6%). 4,5-Diamino-6-methylpyrimidine [10] similarly gave *7-hydroxy-4-methylpteridine* (80%) (colourless crystals from 40 parts of water). This, unlike the 2- and the 6-methyl isomer, rapidly became orange when warmed in air, and was prepared under nitrogen (Found: C 51·5; H 3·6; N, 34·2%).

6-Acetonyl-7-hydroxypteridine.—Ethyl 2,4-dioxopentanoate (0·24 g.) was heated at 98° for 15 min. with 4,5-diaminopyrimidine (0·11 g.) and N-acetate buffer (pH 5; 3·5 ml.). The yellow leaflets which were deposited on cooling were filtered off and the filtrate was reheated with more ester (0·24 g.). The total yield of *6-acetonyl-7-hydroxypteridine*, decomp. about 280°, was 35% (Found, for material recrystallized from water: C, 53·0; H, 3·9; N, 27·4. $C_9H_8N_4O_2$ requires C, 52·9; H, 3·95; N, 27·4%). When heated with N-sodium hydroxide at 98° for 30 min., it gave about equal parts of 7-hydroxy-6-methyl- and 6,7-dihydroxy-pteridine.

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XUM

25. *The Thermal Decomposition of* 1-*Chloroethyl Methyl Ether.*

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The decomposition of 1-chloroethyl methyl ether in the temperature range 180—250° is a homogeneous first-order reaction, the rate constant k_1 being

$$2{\cdot}90 \times 10^{11} \exp(-33{,}300/RT) \text{ sec.}^{-1}$$

The reaction mechanism is the unimolecular elimination of hydrogen chloride. The methoxyl group exerts a large accelerating effect in this type of gas-phase reaction.

The mechanism of unimolecular dehydrohalogenation has been observed in thermal, gas-phase decomposition of a number of alkyl chlorides [1] and bromides.[2] The effect of molecular structure on this type of reaction has been discussed by Maccoll and Thomas [3] who suggest that the important rate-controlling stage is initial polarisation of the carbon–halogen bond, basing this on two general observations: (*a*) the rate of reaction is almost wholly determined by the substituents in the α-position to the carbon–halogen bond, (*b*) the α-substituent effects show a marked parallel with the structural effects exerted by the same substituents in S_N1 and E_1 reactions in polar solvents, suggesting that common electronic effects are involved in both types of reaction.

In the present investigation this hypothesis was tested by studying the effect of an α-methoxyl group on the rate of unimolecular elimination of hydrogen chloride in the particular case of 1-chloroethyl methyl ether. This compound and its analogues readily undergo solvolytic reactions involving nucleophilic displacement of the halogen, in which the mechanism is of the unimolecular S_N1 type.[4] The accelerating effect of the methoxyl group in these reactions can be attributed to mesomeric release of electrons to the developing carbonium-ion centre; [5] a comparable acceleration is now found for the gas-phase molecular elimination of hydrogen chloride.

Experimental

1-Chloroethyl methyl ether, b. p. 72—73°, was prepared as described by Henze and Murchison.[6] The reaction was followed by measuring the rate of change of pressure in a static system. The apparatus and technique have been described previously.[7] Owing to the instability of the chloro-ether, it was not practicable to use a heated vapour-reservoir for admitting the reactant to the reaction vessel. The following method was adopted. A small side-arm was connected to the capillary inlet of the reaction vessel. Before a run this side-arm was immersed in the liquid air, and the required amount of the ether was distilled into it from a reservoir at room temperature. The reaction vessel and side-arm were then isolated from the main system, and the run was started by rapidly " flaming " the material from the side-arm into the reaction vessel. This method avoided heating the bulb containing the ether.

In a clean glass reaction vessel, appreciable decomposition of 1-chloroethyl methyl ether was observed at temperatures as low as 110°. After the walls had been coated with a thin layer of carbon by decomposing allyl bromide in the vessel at 350°, a much slower reaction was observed which was conveniently measurable in the temperature range 180—250°. The homogeneity of the reaction in vessels coated in this manner was established by comparing the rates of decomposition in an unpacked (surface/volume ratio 0·95 cm.$^{-1}$) and a packed reaction vessel (surface/volume ratio 2·8 cm.$^{-1}$). The results are included in Table 4. Only

[1] Barton *et al.*, *J.*, 1951, 2039, and earlier papers there cited; Howlett, *J.*, 1953, 945, and earlier papers there cited.
[2] Maccoll *et al.*, *J.*, 1960, 184 and earlier papers there cited.
[3] Maccoll and Thomas, *Nature*, 1955, **176**, 392.
[4] Ballinger, de la Mare, Kohnstam, and Prestt, *J.*, 1955, 3641.
[5] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 333.
[6] Henze and Murchison, *J. Amer. Chem. Soc.*, 1931, **53**, 4077.
[7] Maccoll and Thomas, *J.*, 1955, 979.

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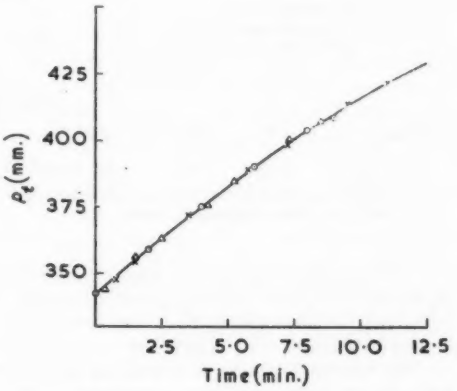
a slight increase in rate was observed in the packed vessel. On condensation, the reaction products recombined quantitatively to yield the original ether. If, during a run, the contents of the reaction vessel were condensed in the side-arm, allowed to warm gradually, and then re-admitted to the reaction vessel, the pressure then observed was equal to the pressure of the ether originally introduced. The subsequent pressure–time curve was also identical with the original curve within the limits of experimental error. A series of pressure–time curves illustrating this behaviour is shown in the Figure. First-order rate constants calculated from the separate curves agree within 4%. Although the rapid recombination of the products prevented their determination by standard analytical methods, the observed behaviour indicates that the forward reaction is the elimination of hydrogen chloride. It also indicated that no appreciable side reaction or further decomposition was involved.

In runs which were followed until no further increase in pressure was detectable, the ratio of the final pressure to the initial pressure was ~1·75. That this ratio was less than 2·0 can be attributed partly to dead-space errors and partly to the establishment of an equilibrium between reactant and products (cf. butyl chloride [8]).



Pressure–time curves demonstrating quantitative recombination of reaction products on condensation.

○, *Original pressure–time curve.*
△, *After condensation and readmission to reaction vessel.*
×, *After condensation and readmission to reaction vessel a second time.*

In previous investigations of this type, the use of pressure measurements to follow the course of the reaction has been justified by showing that the observed pressure change Δp is a direct measure of the amount of hydrogen halide formed. This involved determination of the hydrogen halide in the condensed products by standard analytical methods, a procedure which could not be applied in the present case because of the tendency of the products to recombine. The alternative method of estimating the hydrogen chloride *in situ* by precipitating it as ammonium chloride was adopted. The pressure-change in the system after addition of gaseous ammonia could not be directly related to the amount of hydrogen chloride removed because the equilibrium in the system was disturbed. If, however, ammonia was admitted to the system in measured quantities at time intervals sufficient to allow the system to regain equilibrium, the total pressure in the system decreased until the ether had been completely decomposed and the chloride precipitated. Thereafter, the pressure increased as a direct measure of the excess of ammonia added. If the overall reactions involved are

$$CH_3{\cdot}CHCl{\cdot}OMe \longrightarrow CH_2{:}CH{\cdot}OMe + HCl \quad . . . . . (1)$$

$$HCl + NH_3 \longrightarrow NH_4Cl \quad . . . . . (2)$$

then, at the minimum pressure observed, the pressure of added ammonia and the residual pressure of methyl vinyl ether should both be equivalent to the initial pressure of the chloroether, p_0. The results of four determinations are shown in Table 1. Agreement between the three quantities is reasonable. Appreciable deposits of ammonium chloride were formed in the reaction system which had to be cleaned and recoated between experiments. Mass-spectrometric analysis (kindly performed by Dr. C. J. Danby) of a sample of the gas remaining after the chloride had been precipitated gave a mass-spectral pattern consistent with that of methyl

[8] Howlett, *J.*, 1951, 1409.

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vinyl ether. These observations were added proof that the overall reaction is that represented by (1) above.

TABLE 1. *Temperature* 200°.

p_0 (chloro-ether) (mm.)	148	178	180	264
p (NH_3 added) (mm.)	156	170	166	248
p (min.*) (mm.)	146	176	175	259

* The results have been corrected to allow for the slight dissociation of ammonium chloride.

TABLE 2. *Reaction at* 218·5°.

p_0 (mm.)	420	382	299	242	216	196	189	187	135	92	33
10^4k_1 (sec.$^{-1}$)	4·39	4·22	4·44	4·22	4·54	4·44	4·50	4·46	4·31	4·59	4·82

TABLE 3. *Reaction at* 232°.

p_0 (ether) (mm.)	245	236	243	200	202
p (cyclohexene) (mm.)	—	—	35	40	115
10^4k_1 (sec.$^{-1}$)	11·8	12·2	11·8	12·8	12·6

TABLE 4.

Temp.	188°	201°	206° *	215·5°	218·5°	227° *	232°	245°
No. of runs	7	8	6	8	8	6	8	8
10^4k_1 (sec.$^{-1}$)	0·49	1·26	2·23 (1·84)	3·55	4·39	8·84 (7·94)	12·1	25·9

* Runs in a packed vessel (surface/volume ratio 2·80 cm.$^{-1}$). Values in parentheses are interpolated values for k_1 in the unpacked vessel.

The logarithmic plots were linear for the first 35—40% of the reaction only. Subsequent decrease in the first-order rate was attributed to appreciable reversal of the reaction. First-order rate constants were measured over a wide range of initial pressures (33—420 mm.), as shown in Table 2. No significant variation in the first-order rate constants was observed.

The rate of decomposition was not affected by added cyclohexene (see Table 3) which has been shown to be an effective inhibitor of the chain mechanism of decomposition of several alkyl bromides.

The rate of decomposition was measured at several different temperatures as summarized in Table 4. The variation of the first-order rate constant with temperature is given by the Arrhenius equation

$$k_1 = 2{\cdot}90 \times 10^{11} \exp(-33{,}300/\boldsymbol{R}T) \text{ sec.}^{-1}$$

DISCUSSION

The experimental results establish that the thermal decomposition of 1-chloroethyl methyl ether in the temperature range 180—250° is a homogeneous, first-order reaction. The overall reaction is the elimination of hydrogen chloride and the formation of methyl vinyl ether (reaction 1 above).

The low activation energy, the absence of side reactions, and the lack of inhibition by added cyclohexene indicate that reaction does not proceed by a free-radical mechanism either of a chain or of a non-chain character. It is concluded, therefore, that the mechanism is direct loss of molecular hydrogen chloride, a conclusion consistent with the observed kinetic behaviour. The decomposition is thus another example of the unimolecular dehydrohalogenation observed in the decomposition of numerous alkyl bromides and chlorides.

Decomposition in a manner analogous to that of alkyl ethers would have involved one or both of the following reactions:

$$CH_3{\cdot}CHCl{\cdot}OMe \longrightarrow CH_3{\cdot}COCl + CH_4$$

$$CH_3{\cdot}CHCl{\cdot}OMe \longrightarrow CH_3{\cdot}CH_2Cl + CH\,O$$

No evidence for the occurrence of either of these reactions was obtained. In this respect the chloro-ether behaves as a typical halide, and the methoxyl group is not directly involved in the rearrangement.

The effect of the methoxyl group on the rate of unimolecular dehydrochlorination may be assessed by comparing the Arrhenius parameters and the relative rate of decomposition of 1-chloroethyl methyl ether with those of other alkyl chlorides,[9] as in Table 5. The relative rates of decomposition at 330° have been calculated from the Arrhenius equations. An intermediate temperature was chosen in order to minimise errors of extrapolation.

TABLE 5.

Compound	log A	E (kcal. mole^{-1})	Rel. rate at 330°	Compound	log A	E (kcal. mole^{-1})	Rel. rate at 330°
$CH_3{\cdot}CH_2Cl$	14·6	60·8	1	$(CH_3)_2CCl$	12·41	41·2	$7{\cdot}1 \times 10^4$
$CH_3{\cdot}CH_2{\cdot}CH_2Cl$	13·45	55·5	6·0	Me·CHCl·OMe ...	11·46	33·3	$6{\cdot}9 \times 10^6$
$(CH_3)_2CHCl$ ...	13·40	50·5	$3{\cdot}7 \times 10^2$				

Substituent effects are most conveniently discussed in terms of α- and β-substitution in ethyl chloride, the simplest chloride which can undergo decomposition by the unimolecular mechanism. Introduction of an α-methoxyl group markedly lowers the activation energy and correspondingly increases the rate of decomposition greatly. The effect of the methoxyl group is much greater than that of an α-methyl group (isopropyl chloride) or the combined effect of two α-methyl groups (t-butyl chloride).

Although still within the range considered " normal " for unimolecular reactions, the value of log A for 1-chloroethyl methyl ether is lower than those reported for the other chlorides. This result agrees with the observation by Barton and his co-workers that a positive linear relation holds between log A and E for this series of reactions. No such relation was observed in the corresponding reactions of the alkyl bromides, although in other respects the two series of reactions are very similar. The possible significance of a relation of this type is outside the scope of the present discussion. The variation in log A is in any case small compared with the variation in E, and the substituents influence reactivity primarily by altering the latter.

Unimolecular solvolyses (S_N1 mechanism) of a series of chloro-ethers have been studied by de la Mare and his co-workers.[4] By combining their results with others these authors give the following approximate estimate of relative reactivities in the temperature range 0—100° c: $CH_3{\cdot}CH_2{\cdot}CH_2Cl$ 1, $(CH_3)_3CCl$ 10^7, $MeO{\cdot}CH_2Cl$ 10^{13}, $CH_3{\cdot}CHCl{\cdot}OMe$ $>10^{15}$. Comparison of these figures with the relative rates of the gas-phase reactions (Table 5) reveals a qualitative similarity of substituent effects in the two types of reaction. The magnitude of the rate difference for a given substituent is much smaller in the gas-phase reaction, but this is largely due to the much higher temperature at which the latter have been studied. If the relative rates of unimolecular elimination of n-propyl chloride and 1-chloroethyl methyl ether at 0° are compared the rate ratio is $1 : 10^{16}$, which is of the same order of magnitude as the difference observed in the corresponding solution reactions.[10] The quantitative similarity of the acceleration effected by the methoxyl group is a very strong indication that both reactions involve the same type of electron-displacements. The reactions in solution undoubtedly involve heterolysis of the carbon–chlorine bond. The corresponding change in the gas-phase mechanism would be a partial or complete polarisation of the bond during the rate-determining stage of the reaction. (Heterolytic dissociation into separate ions in the gas phase is not feasible at the experimental temperature on energetic grounds and it is not suggested that this occurs.)

The decomposition of 1-chloroethyl methyl ether thus affords a further striking example of the general parallel between unimolecular dehydrohalogenation in the gas phase and

[9] Barton and Howlett, *J.*, 1949, 165; Barton, Head, and Williams, *J.*, 1951, 2039; Barton and Head, *Trans. Faraday Soc.*, 1950, **46**, 114; Barton and Onyon, *Trans. Faraday Soc.*, 1949, **45**, 725.
[10] Ingold, *Proc. Chem. Soc.*, 1957, 279.

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the S_N1 and $E1$ reactions of the same compounds in polar solvents, and supports the hypothesis that the rate-determining stage in the gas phase involves a polar transition state.

This work was completed during the tenure of an Imperial Chemical Industries Fellowship. The author thanks Professor Sir Cyril Hinshelwood, P.R.S., for much valuable encouragement and advice and Drs. A. Maccoll and P. B. de la Mare for many helpful discussions.

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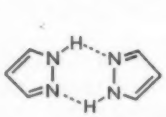
26. *The Hydrogen Bonding of Pyrazole in Carbon Tetrachloride Solution.*

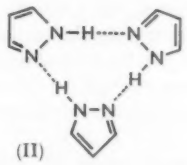
By D. M. W. ANDERSON, J. L. DUNCAN, and F. J. C. ROSSOTTI.

Analysis of the concentration-dependence of the infrared spectrum of pyrazole in carbon tetrachloride at 18° ± 1° has shown that the fundamental N–H stretching band at 3485 ± 10 cm.$^{-1}$ is due to monomeric pyrazole only. Hydrogen-bonding equilibria in the concentration range 10^{-4}—1M have been interpreted quantitatively in terms of co-existing monomer, cyclic dimer, and cyclic trimer, with overall formation constants of $\beta_{20} = 47{\cdot}5 \pm 1{\cdot}0$ l. mole^{-1} and $\beta_{30} = 7540 \pm 240$ l.^{2} mole^{-2}.

HÜCKEL and his co-workers [1] have suggested, on the basis of cryoscopic, viscometric, and dielectric measurements, that pyrazole consists predominantly of a cyclic, hydrogen-bonded dimer (I) at moderate concentrations in non-associated solvents. It was also suggested that more than two monomers might form chains at higher concentrations.



(I)



(II)

Hunter [2] has recently criticised the non-linear hydrogen bond in (I) and suggested that the strainless cyclic trimer (II) would be more stable. A cryoscopic study of 3,5-dimethylpyrazole in benzene by White and Kilpatrick [3] has given convincing evidence for the existence of a stable trimer, and dubious evidence for an unstable dimer. These authors consider that the trimer is almost certainly cyclic, and the dimer most probably linear. An *X*-ray analysis by Ehrlich [4] has now shown that pyrazole exists in the solid state as long, parallel, hydrogen-bonded chains, which describe figure-of-eight spirals. The present study was undertaken to investigate the nature of the pyrazole oligomers which exist in carbon tetrachloride solution.

A preliminary study of dilute solutions of pyrazole in carbon tetrachloride showed a fundamental N–H stretching mode at 3485 ± 10 cm.$^{-1}$ with a half-band width of 20 cm.$^{-1}$. The intensity of this band decreased with increasing total concentration, B; concurrently, a broad, bonded N–H band of increasing intensity appeared in the region 3400—2000 cm.$^{-1}$

[1] Hückel, Datow, and Simmersbach, *Z. phys. Chem.*, 1940, **186**, *A*, 129; Hückel and Jahnentz, *Ber.*, 1942, **75**, 1438.
[2] Hunter, in " Progress in Stereochemistry," ed. Klyne, Butterworths, London, 1954, p. 223.
[3] White and Kilpatrick, *J. Phys. Chem.*, 1955, **59**, 1044.
[4] Ehrlich, *Acta Cryst.*, 1960, **13**, 946.

Bonded N–H *absorption bands of pyrazole (all peaks strong)*

Solid (cast film)	3135	3050	2960	2900	2860	2810(sh)
CCl_4 solution	3175	3070	2995	2930	2905	2825(sh)

(see Fig. 1); this showed six major peaks [excluding that due to C–H at 3120 cm.$^{-1}$ (w)], which were remarkably similar to the infrared N–H absorption bands of a solid, cast film of pyrazole. A quantitative study was therefore made of the concentration-dependence of the intensity of the 3485 cm.$^{-1}$ band.

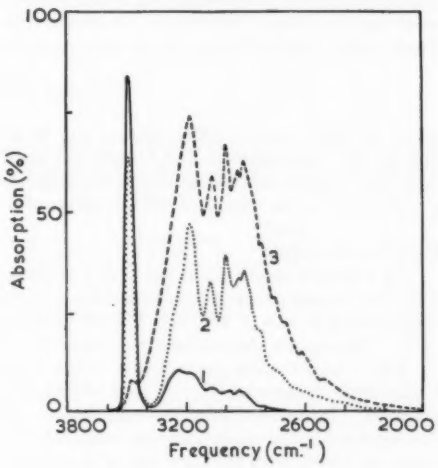


FIG. 1. *Infrared absorption spectra in the region 3800—2000 cm.$^{-1}$ for carbon tetrachloride solutions of pyrazole at various total concentrations, B, at 18°.*

1, $B = 0{\cdot}001$M. 2, $B = 0{\cdot}010$M.
3, $B = 1{\cdot}00$M.

EXPERIMENTAL

Materials.—Pyrazole was recrystallised twice from cyclohexane; it had m. p. 70° (lit., 70°). Reagent-grade carbon tetrachloride was used without further purification; no O–H absorption spectrum was detectable on using 4 cm. cells.

Infrared Measurements.—The spectrophotometer was a Hilger H800 double-beam instrument. A rock-salt prism was used for preliminary studies, and a quartz prism for precise measurements on dilute solutions ($B < 10^{-2}$M). The quartz prism gave a theoretical slit-width of 8 cm.$^{-1}$ at 3485 cm.$^{-1}$ with a spectrometer slit-width of 0·30 mm. The frequency scale was calibrated with reference to the N–H stretching frequency of pyrrole vapour (3530 cm.$^{-1}$). The spectrophotometer was not thermostatically controlled, and wave-number estimates are

TABLE 1. *Infrared absorbancies at 3485 cm.$^{-1}$ of associated pyrazole in carbon tetrachloride at 18° ± 1°.*

10^4B ...	0·9947	1·989	2·984	3·979	4·974	5·968	6·963	7·958	8·952	9·947
$\log I_0/I$...	0·0894 *	0·174 *	0·260 *	0·347 *	0·417 *	0·494 *	0·574 *	0·646 *	0·721 *	0·0985
10^4B.....	11·94	13·93	15·92	17·91	19·89	21·88	23·87	25·86	27·85	29·84	31·83
$\log I_0/I$...	0·118	0·134	0·150	0·167	0·179	0·193	0·210	0·222	0·235	0·244	0·257
10^4B.....	33·82	35·81	37·80	39·79	41·78	43·77	45·76	47·75	49·74	51·72	53·71
$\log I_0/I$...	0·271	0·287	0·295	0·305	0·314	0·329	0·336	0·346	0·351	0·363	0·373
10^4B.....	55·70	57·69	59·68	61·67	63·66	65·65	67·64	69·63	79·58	89·52	99·47
$\log I_0/I$...	0·385	0·394	0·399	0·408	0·419	0·426	0·434	0·438	0·478	0·507	0·539

* 4·00 cm. cells: all other results refer to 0·500 cm. cells.

considered to be accurate to ±10 cm.$^{-1}$ within the region 3500—3000 cm.$^{-1}$. Run-to-run reproducibility was ±5 cm.$^{-1}$. Instrumental conditions were: gain, 4; damping, 2; speed of scan, 68 cm.$^{-1}$/min. Variable path-length cells, set at 5·000 ± 0·005 mm. and fitted with

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rock-salt windows, were used for most of the measurements. However, a carefully matched pair of 4·00 cm. Unicam quartz cells was necessary for the most dilute solutions. Evaporation losses were negligible. The instrument was operated with pure solvent in the reference beam.

Two stock 0·09947M-solutions of pyrazole in carbon tetrachloride were prepared by semi-micro-weighing. Subsequent dilution was effected by using an Agla micrometer syringe. More concentrated solutions ($B > 0{\cdot}1$M) were prepared by direct weighing. No interaction between the pyrazole and decomposition products of the solvent was detectable. Solution temperatures were 18° ± 1°.

Procedure.—By using 4·00 cm. cells in the concentration range $1 \times 10^{-4} \leqslant B \leqslant 4 \times 10^{-4}$M, where no hydrogen bonding was detectable, the intensities of the free N–H band at 3485 cm.$^{-1}$ were found to obey Beer's law. A mean value of $\varepsilon = 220 \pm 3$ was obtained for the apparent molar extinction coefficient of the monomer, on using the relation

$$\log (I_0/I) = \varepsilon e l \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where I_0 and I are the intensities of the incident and transmitted radiation, e is the free N–H end-group concentration, and l is the cell length. In measuring the ratio I_0/I, frequent checks were made upon the constancy of the absorption base-line. The value of ε was also obtained graphically as $\lim_{B \to 0} (\log I_0/I)/Bl$: a value of $\varepsilon = 220 \pm 2$ was found, in good agreement with the previous value.

As a further check upon the optics of the system, it was confirmed that the intensity of the 3485 cm.$^{-1}$ band adhered to Lambert's law in the region where hydrogen bonding was detectable. Solutions of $B = 8 \times 10^{-4}$ and 1×10^{-3}M were used in conjunction with the 4·00 and 0·500 cm. cells. The results obeyed Lambert's law to ±1%.

The concentration dependence of the intensity of the 3485 cm.$^{-1}$ band was then studied. Forty-three solutions ($10^{-4} \leqslant B \leqslant 10^{-2}$M) were prepared in duplicate, one from each stock solution. Intensities were reproducible to ±1%, and the mean values are given in Table 1. Intensities for the concentration range $10^{-2} \leqslant B \leqslant 1$M were less precise, as the bonded N–H band interfered with the base line of the free N–H band. These data are therefore not reported.

Interpretation of the Data

It cannot be assumed *a priori* that the free N–H band at 3485 cm.$^{-1}$ in associated pyrazole solutions is due to the monomer only.[5,6] It is, however, valid to assume that the band is due to free N–H end-groups, and, further, that the apparent molar extinction coefficients of all linear oligomers B_q are equal. End-group concentrations, e, were therefore calculated by using the experimental value of $\varepsilon = 220 \pm 3$ for the monomer. Overall association constants are defined as

$$\beta_{q0} = B_q/b^q \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where B_q is the concentration of B_q, and b the concentration of monomer. For simplicity, we anticipate our conclusions by limiting subsequent consideration to monomeric, dimeric, and trimeric species. Two mass-balance expressions follow from eqn. (2):

$$B = B_1 + 2B_2 + 3B_3 = b + 2\beta_{20}b^2 + 3\beta_{30}b^3 \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$S = B_1 + B_2 + B_3 = b + \beta_{20}b^2 + \beta_{30}b^3 \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where S is the sum of the concentrations of all species. It was found that the experimental data could be represented by the linear equation

$$(B - e)/e^2 = 22{,}620e + 94{\cdot}8 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

[5] Coggeshall and Saier, *J. Amer. Chem. Soc.*, 1951, **73**, 5414; Huggins and Pimentel, *J. Phys. Chem.*, 1956, **60**, 1615; Coburn and Grunwald, *J. Amer. Chem. Soc.*, 1958, **80**, 1318.

[6] Pimentel and McClellan, "The Hydrogen Bond," Freeman and Co., San Francisco, 1960, pp. 97, 207.

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The standard deviations of the slope and intercept were found to be ± 716 and ± 2 by an unweighted least-squares treatment.

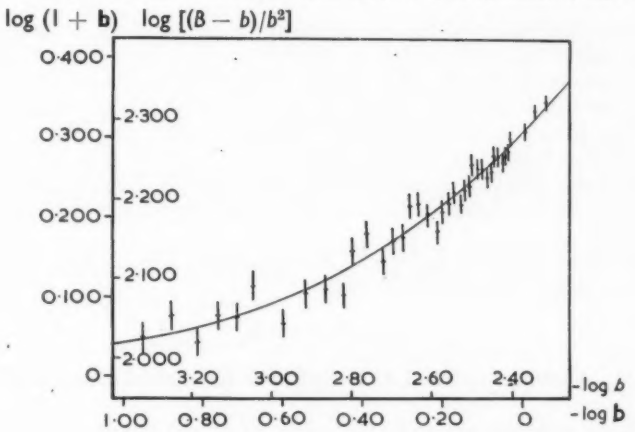
The significance of the experimental eqn. (5) follows from a consideration of the four possible combinations of linear and cyclic oligomers, B_2 and B_3. The experimental variables $(B - e)/e^2$ and e are expressed in terms of b by using eqns. (3) and (4) for the four possibilities in Table 2.

TABLE 2. *The possible variables of eqn.* (5) *for the pyrazole system in carbon tetrachloride.*

B_2	B_3	$(B - e)/e^2$	e
Cyclic	Cyclic	$2\beta_{20} + 3\beta_{30}b$	b
Linear	Linear	$(\beta_{20} + 2\beta_{30}b)/(1 + \beta_{20}b + \beta_{30}b^2)^2$	$b + \beta_{20}b^2 + \beta_{30}b^3$
Cyclic	Linear	$(2\beta_{20} + 2\beta_{30}b)/(1 + \beta_{30}b^2)^2$	$b + \beta_{30}b^3$
Linear	Cyclic	$(\beta_{20} + 3\beta_{30}b)/(1 + \beta_{20}b)^2$	$b + \beta_{20}b^2$

It is apparent that $(B - e)/e^2$ will be linear in e if the free N–H band is in fact due to monomeric pyrazole only, and the dimer and trimer are both cyclic. However, it is

FIG. 2. *The experimental data log* $[(B - b)/b^2]$ *plotted as a function of* log b *superimposed in the position of best fit on the normalised curve* log $(1 + \mathbf{b})$ *as a function of* log **b**.



extremely unlikely that a linear representation of the data according to eqn. (5) would have been found, if either or both the associated species were linear. We therefore derive from eqn. (5) values of

$$\beta_{20} = 47{\cdot}4 \pm 1{\cdot}0 \text{ l. mole}^{-1} \text{ and } \beta_{30} = 7540 \pm 240 \text{ l.}^2 \text{ mole}^{-2}$$

The values of the association constants were checked by the curve-fitting method suggested by Rossotti and Rossotti.[7] The expression

$$\log\left(\frac{B - b}{b^2}\right) - \log 2\beta_{20} = \log\left(1 + \frac{3\beta_{30}}{2\beta_{20}}\,\mathrm{b}\right)$$

is a rearrangement of eqn. (3). The experimental data, log $\{(B - b)/b^2\}$ plotted as a function of log b, will therefore be of the same shape as the normalised curve log $(1 + \mathbf{b})$

[7] Rossotti and Rossotti, " The Determination of Stability Constants," McGraw-Hill, New York, in the press, Chap. 16.

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plotted as a function of log **b**. The experimental and normalised curves are superimposed, and, in the position of best fit (see Fig. 2), the equations

$$\log (1 + \mathbf{b}) = \log [(B - b)/b^2] - \log 2\beta_{20}$$

and

$$\log \mathbf{b} = \log b + \log (3\beta_{30}/2\beta_{20})$$

may be solved for β_{20} and β_{30}/β_{20}. The permissible relative displacements of the experimental and the normalised curves, parallel to the co-ordinate axes, give estimates of the errors in the two parameters. Hence, we obtain values of

$$\beta_{20} = 47{\cdot}5 \pm 1{\cdot}0 \text{ l. mole}^{-1} \text{ and } \beta_{30} = 7540 \pm 300 \text{ l.}^2 \text{ mole}^{-2}$$

in excellent agreement with the values obtained from the linear equation. This treatment therefore confirms that monomer, cyclic dimer, and cyclic trimer are the only species co-existing in the concentration range $10^{-4} \leqslant B \leqslant 10^{-2}$ M. There is no evidence for detectable concentrations of larger oligomers.

Discussion

The percentage distribution of pyrazole between the monomer, cyclic dimer, and cyclic trimer has been calculated as a function of the total concentration of pyrazole by using eqn. (3), and is shown in Fig. 3. The precise infrared measurements from which the equilibria have been deduced only extend up to $B = 10^{-2}$M, where the pyrazole is approximately 25% dimeric and 37% trimeric. However, the percentages of monomer, which may be derived from the less precise data in the range $10^{-2} \leqslant B \leqslant 1$M, are in good agreement ($\pm 4\%$) with the values calculated by using eqn. (3). Our values of β_{20} and β_{30} therefore represent the pyrazole system at 18° in carbon tetrachloride for total concentrations $B \leqslant 1$M.

It is evident from the value of β_{20} and β_{30} that the trimer is much more stable than the dimer. The equilibrium constant for the reaction

$$B_2 + B_1 \rightleftharpoons B_3$$

is given by $\beta_{30}/\beta_{20} = 159 \pm 6$ l. mole^{-1}, as compared to the dimerisation constant of 47·5 l. mole^{-1}.

As the pyrazole molecule is planar, the cyclic dimer and trimer will also be planar. Consideration of Ehrlich's structure [4] for the long chains of pyrazole molecules in the solid state suggests that the N–H–N bond in the cyclic trimer may not be quite linear.

An examination of the bonded N–H region, from the viewpoint of the calculated distribution of pyrazole oligomers, suggests that the bands at 3175, 3070, 2995, 2930, 2905, and 2825 cm.$^{-1}$ may be assigned to the trimer. The relative intensities of these bands remain unchanged as B varies. The dimer appears to contribute a leading edge to the band at 3175 cm.$^{-1}$. This absorption becomes a significant shoulder when $B < 10^{-2}$M, and the concentration of dimer exceeds that of trimer. However, the absorption of the trimer is much stronger than that of the dimer, and the shoulder is not detectable for $B > 10^{-2}$M (cf. Figs. 1 and 3). The absorption band of the dimer would be expected to be at a higher frequency than that of the trimer on the basis of Badger's correlation [8] of frequency shift with the energy of the hydrogen bond. Moreover, it has been shown [9] that non-linear intramolecular hydrogen bonds are associated with smaller frequency shifts than linear hydrogen bonds. The frequency shifts for both dimer and trimer clearly correspond to

[8] Badger, *J. Chem. Phys.*, 1940, **8**, 288.
[9] Nakamoto, Magoshes, and Rundle, *J. Amer. Chem. Soc.*, 1955, **77**, 6480.

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very short N–H–N bond lengths (cf. ref. 9). Indeed, the figure-of-eight spirals of pyrazole in the solid state [4] contain N–H bonds of length ~2·9 Å. The shortness of these bonds, and also the tendency to self-association in solution, are presumably both due to a markedly unequal distribution of charge on the two nitrogen atoms of a molecule of pyrazole. The assignment of six bands in the bonded N–H region to a single species is of some interest in connection with current theories of the structure of X–H stretching modes.[10,11]

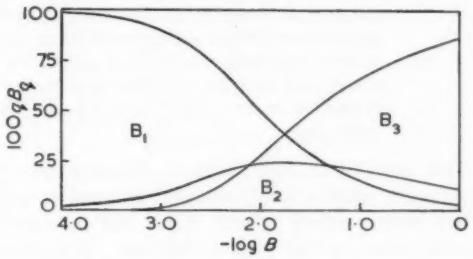

FIG. 3. *The percentage distributions* $100qB_q/B$ *of the pyrazole species in carbon tetrachloride at* 18° *plotted as a function of* log B.

The intensities of the observed N–H bands were markedly sensitive to temperature. With increase of temperature, the intensity of the 3485 cm.$^{-1}$ band due to free pyrazole increased, and that of the broad, bonded N–H band decreased. This implies that the enthalpy changes on association are negative, always provided that the temperature variation of the apparent extinction coefficients is not a dominant factor.[12] As the temperature coefficient of the dielectric constant of carbon tetrachloride is approximately zero,[13] the negative enthalpies appear to be partly due to non-environmental exchange forces. It is therefore possible that the covalent contribution to the hydrogen bond is more important than is commonly supposed.

The infrared spectra of pyrazole in other non-associated solvents, *e.g.*, carbon disulphide and chloroform, are qualitatively similar to that in carbon tetrachloride. It is therefore likely that the same equilibria obtain.

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[10] Bratož and Hadži, *J. Chem. Phys.*, 1957, **27**, 991; Pimentel and McClellan, ref. 6, p. 102.
[11] Sheppard, in "Hydrogen Bonding," eds. Hadži and Thompson, Pergamon Press, London, 1959, p. 85.
[12] Becker, in ref. 11, p. 155; Pimentel and McClellan, ref. 6, p. 76.
[13] Landolt-Börnstein, "Tabellen," II, (6), "Elektrische Eigenschaften 1," Springer-Verlag, Berlin, 1959, p. 625.

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27. *Liquid-phase Reactions at High Pressures. Part XIII.*[1] *Structural Effects in the Acceleration of Menschutkin Reactions by Pressure.*

By A. P. Harris and K. E. Weale.

The rates of a series of Menschutkin reactions have been measured at pressures up to several thousand atmospheres. The extent to which the reactions are accelerated by pressure depends on the molecular structure of the reactants and on the solvent. The theory that the structural variations arise directly from steric interference between non-bonded atoms and groups in the transition state is not supported by our results. The variations are attributed, instead, to differences in the degree and type of solvation of the transition states, which are imposed by the configurations of the reacting molecules.

The rates of reaction between tertiary amines and organic halides to form quaternary salts are substantially increased by pressures of a few thousand atmospheres. The effect has been studied several times but agreement has not been reached on the relative importance of the various factors. Variations in the structures of the reactants alter the amount of the acceleration considerably, but little systematic work has been available on this point. We have measured the effect of pressure on the rates of a series of Menschutkin reactions in order to examine in more detail the influence of structural changes and to obtain more information about the transition states of the reactions.

Experimental

Apparatus and Procedure.—The high-pressure equipment used was similar to that described in an earlier paper,[2] and the reactants were contained in a glass tube with a mercury seal. The same general procedure and method of analysis were used. Two 2 ml. portions were titrated after each run, and the determinations always agreed within 1%. The runs at 1 atm. were carried out in sealed ampoules of amber glass.

Materials.—Methanol. " AnalaR " methanol was purified by the Lund–Bjerrum method, as in previous work [2] (b. p. 64·7°).

Alkyl iodides. These were purified by the method previously used for methyl iodide and stored over triply distilled mercury in a desiccator in the dark. The b. p.s were methyl 42·8°, ethyl 72·2°, n-butyl 131°, isopropyl 89·5°.

Dimethylaniline. " AnalaR " dimethylaniline was refluxed with acetic anhydride for 24 hr. and fractionated. The middle fraction was dried (KOH), re-fractionated under reduced pressure (b. p. 95°/30 mm.) and stored under a vacuum.

NN-*Dimethylbenzylamine.* Purified as above, this had b. p. 181°.

Quinoline. Distilled (b. p. 238°), dried (KOH), and fractionated under reduced pressure (b. p. 110°/14 mm.).

Tri-n-propylamine. The " AnalaR " product, dried (KOH) and fractionated, had b. p. 156·5°.

Nitrobenzene. " AnalaR " nitrobenzene, distilled, dried (Na_2SO_4), and fractionated, had b. p. 210·8°.

Results.—Measurements were made on seven reactions in methanol as solvent and one in nitrobenzene. The reactions of s- and t-butyl iodide with dimethylaniline in methanol were also examined, but satisfactory rate constants could not be obtained because of olefin formation.

The initial concentration of each reactant was 0·1M except for the reactions of *NN*-dimethylbenzylamine and tri-n-propylamine with ethyl iodide in which they were 0·05M. In two cases the second-order rate constants increased as the reaction proceeded, a phenomenon reported by Laidler and Hinshelwood [3] and attributed to autocatalysis by the quaternary salt. In the reaction between dimethylaniline and n-butyl iodide the increase was about 20% at 50%

[1] Part XII, Kilroe and Weale, *J.*, 1960, 3849.
[2] Weale, *J.*, 1954, 2959.
[3] Laidler and Hinshelwood, *J.*, 1938, 858.

TABLE 1. *Second-order rate constants (k in l. mole^{-1} sec.$^{-1}$).*

P (atm.)	Temp.	10^5k	*A* (10^6 sec.$^{-1}$)	*E* (kcal. mole^{-1})
Dimethylaniline + MeI				
1	25·0°	5·62	10·5	15·4
,,	30·0	8·40		
,,	35·0	12·6		
,,	40·0	19·1		
1500	52·5	154		
2875	17·5	20·5	87·1	15·5
,,	18·7	22·9		
,,	19·6	24·7		
,,	22·3	31·8		
,,	25·3	41·0		
Dimethylaniline + EtI				
1	38·9	1·00	8·67	17·1
,,	42·5	1·37		
,,	47·3	2·07		
,,	52·5	3·18		
1500	52·5	12·0		
2875	33·8	5·57	98·2	17·2
,,	38·9	8·79		
,,	47·3	17·8		
,,	52·5	27·7		
4925	33·8	11·7	155	17·0
,,	38·9	18·6		
,,	47·3	37·5		
,,	52·5	57·6		
Dimethylaniline + Bu^{n}I		(10^6k)		
1	47·1	4·66	10·8	18·1
,,	53·0	7·78		
,,	58·0	11·9		
,,	63·5	18·6		
1500	52·5	28·5		
2875	39·0	20·6	99·5	18·1
,,	43·0	29·5		
,,	47·5	43·8		
,,	57·6	106		
Dimethylaniline + Pr^{i}I				
1	45·0	6·26	650	20·4
,,	50·0	10·3		
,,	55·0	16·7		
,,	57·8	21·7		
1500	52·5	72·7		
2875	45·0	90·4	7360	20·25
,,	50·0	147		
,,	55·0	240		
,,	58·5	330		

P (atm.)	Temp.	10^5k	*A* (10^6 sec.$^{-1}$)	*E* (kcal. mole^{-1})
Quinoline + EtI				
1	42·6°	4·88	940	20·6
,,	47·6	8·28		
,,	52·5	13·3		
,,	57·5	20·0		
1500	52·5	32·6		
2875	42·6	21·3	11,000	21·3
,,	47·6	35·6		
,,	52·5	58·1		
,,	57·5	91·2		
Dimethylbenzylamine + EtI		(10^4k)		
1	42·5	1·33	182	17·5
,,	47·5	2·05		
,,	52·5	3·10		
,,	57·5	4·69		
1500	52·5	8·56		
2875	42·6	7·38	250	16·7
,,	47·6	11·3		
,,	52·3	16·6		
,,	57·5	24·0		
Tri-n-propylamine + EtI		(10^5k)		
1	42·5	1·68	725	19·7
,,	47·7	2·88		
,,	52·5	4·47		
,,	57·5	6·96		
1500	42·8	5·02	2500	19·8
,,	47·5	8·55		
,,	52·5	14·0		
,,	57·5	20·5		
2875	42·5	11·4	1620	18·99
,,	47·5	18·8		
,,	52·5	28·2		
,,	57·5	46·0		
Dimethylaniline + EtI (in nitrobenzene)				
1	47·5	1·63	0·0128	13·05
	52·5	2·24		
	57·5	3·08		
1500	52·5	6·15		
2300	,,	9·51		
2600	,,	11·3		

conversion, and it was somewhat larger for the reaction between dimethylaniline and isopropyl iodide. In both cases the rate constant was found to be a linear function of the percent conversion, and satisfactory values were obtained by extrapolation to zero conversion.

The reaction in nitrobenzene reached equilibrium at about 60% conversion and this was taken into account in calculating the rate constants.

The rate constants were corrected for the compressibility of the solvent. The most accurate data available for methanol are Gibson's [4] which were determined at 25° and up to 1000 atm. Compressions at higher pressures and other temperatures were calculated by the procedure of Bett, Newitt, and Weale [5] with Larionov's sound-velocity data.[6] At 1 atm. and 25° the agreement between Gibson's measurements and Larionov's is within 0·01%. Gibson and Loeffler's

[4] Gibson, *J. Amer. Chem. Soc.*, 1935, **57**, 1551.
[5] Bett, Newitt, and Weale, *Brit. J. Appl. Phys.*, 1954, **5**, 243.
[6] Larionov, *Zhur. fiz. Khim.*, 1953, **27**, 1002.

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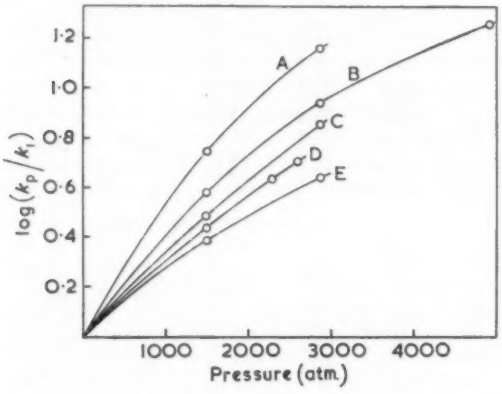
compression data for nitrobenzene [7] can be accurately interpolated at different temperatures, and the correction for this solvent was calculated from the constants obtained by them for the Tait equation. The corrected rate constants are given in Table 1, together with rounded-off Arrhenius parameters. The rate constants for the reaction between dimethylaniline and methyl iodide at 1 atm. agree well with values determined by Evans, Watson, and Williams.[8] The constants for the reaction between dimethylaniline and ethyl iodide in methanol at 1 atm. are in reasonable agreement with those of Brown and Fried,[9] but the constant at 25° measured by Hamann and Teplitzky [10] appears slightly too high.

Discussion

General.—All the reactions are substantially accelerated by pressure. At 52·5° the ratio k_{2875}/k_1 varies from 14·4 ($NPhMe_2 + Pr^nI$) to 4·4 (quinoline + EtI). The rate constants at 1 atm. vary with the nature of the reaction by a factor of about 50 and there



Effect of pressure on $\log k_p/k_1$.
Reactions of dimethylaniline with (A) *isopropyl iodide,* (B) *ethyl iodide, and* (C) *methyl iodide, all in methanol, and* (D) *with ethyl iodide in nitrobenzene; also* (E) *of quinoline with ethyl iodide.*

appears to be no correlation between them and the pressure effect. In the reaction between dimethylaniline and the four iodides acceleration with pressure increases in the order Me < Et ≈ Bu < Pr^i, confirming Perrin and Williams's [11] observation that it is greater for the more complex reactants.

Interpretations of the Pressure Effect.—The variation of rate constant with pressure is given by the equation

$$(\delta \ln k/\partial P)_T = -\Delta V^*/RT$$

where ΔV^* is the molar volume change when the reactants are converted into the transition state. ΔV^* has negative values for reactions which are accelerated by pressure. The curvature of the plots of $\log k_p/k_1$ against pressure obtained from our experimental results (see Figure) shows that the changes of volume become less and that the rate constants increase more and more slowly at higher pressures. Evans and Polanyi [12] pointed out that ΔV^* includes a term representing the different degrees of solvation of reactants and transition state. Eyring and his co-workers [13] neglected this term in calculating ΔV^* for two Menschutkin reactions, but evidence has accumulated [14] that in ion-producing

[7] Gibson and Loeffler, *J. Amer. Chem. Soc.*, 1939, **61**, 2515.
[8] Evans, Watson, and Williams, *J.*, 1939, 1345, 1348.
[9] Brown and Fried, *J. Amer. Chem. Soc.*, 1943, **65**, 1841.
[10] Hamann and Teplitzky, *Discuss. Faraday Soc.*, 1956, **22**, 114.
[11] Perrin and Williams, *Proc. Roy. Soc.*, 1937, *A*, **159**, 162.
[12] Evans and Polanyi, *Trans. Faraday Soc.*, 1935, **31**, 875; 1936, **32**, 1333.
[13] Glasstone, Laidler, and Eyring, " The Theory of Rate Processes," McGraw-Hill, New York, 1941, p. 472.
[14] Hamann, " Physico-Chemical Effects of Pressure," Butterworths, London, 1957.

reactions the greater part of ΔV^* is due to the volume changes accompanying increased solvation. It has frequently been assumed that in Menschutkin reactions the transition state is solvated to about the same extent as the product ions, but Gonikberg and Povkh [15] have advanced a different view, based on the effect of pressure on the reaction between ethyl iodide and pyridine in acetone. They estimated ΔV^* at 1 atm. and 30° to be −20 c.c./mole, whereas ΔV_s, the total volume change for the reaction in solution, is −54 c.c./mole in acetone.[16] They also measured the molar volume of the pure (unsolvated) liquid product and calculated the total volume change ΔV_0 in the absence of solvent to be −20·5 c.c./mole at 30°. Their conclusion that the transition state is not solvated as completely as the product ions has been criticised by Hamann,[17] chiefly on the ground that ΔV^* at 1 atm. cannot be estimated accurately from a curve of the type shown in the Figure if there are no experimental points below 3000 atm. To meet this objection Gonikberg and Zhulin [18] measured the rate of the same reaction in acetone at 40° and at 1, 250, 500, 750, 1000, and 3000 atm. The new value obtained for ΔV^* at 1 atm. is -30 ± 1 c.c./mole, and ΔV_s at 20° was redetermined and found to vary between −58 and −54 c.c./mole as the reaction proceeded. The improved measurements still indicate that the transition state is less solvated than the quaternary salt and while it is possible that the graph of log k_p/k_1 against pressure shows increased curvature in the range 1—250 atm. it is probable that there is a significant difference between ΔV^* and ΔV_s. This is not surprising as the ionic charges in the transition state may not be fully developed and the ions have not separated sufficiently to permit formation of a complete solvent shell. Gonikberg and Zhulin's experimental points below 1000 atm. can be well predicted from a smooth curve of minimum curvature drawn through the points at 3000 and 1000 atm. and the origin. Therefore curves of this type have been drawn through the experimental points of the Figure and used to estimate the values of ΔV^* at 1 atm. in Table 2, which are discussed below. For the reaction between ethyl iodide and tri-n-propylamine ΔV^* is −24 c.c./mole and in this case we have determined ΔV_s at 19·6°, by a dilatometric method, to be −56·6 c.c./mole, so that a similar difference between the two quantities occurs in methanol.

As supporting evidence that the transition state in Menschutkin reactions is incompletely solvated the differences between entropies of activation ΔS^*, and the overall entropy change, ΔS, have been cited. Syrkin and Gubareva [19] give results which show that $-\Delta S$ is usually larger that $-\Delta S^*$ by 5 to 15 e.u., and the difference is greater if the entropy of activation is corrected for the "cratic" term (see p. 151). However, in the reaction between dimethyl-*o*-toluidine and methyl iodide in acetone [20] ΔS^* and ΔS at 44° are −40 (uncorrected) and −32·1 respectively. This anomaly can be attributed to steric strain in the activated complex, and to hindered solvation of the charged nitrogen atom.

The only study of a reverse Menschutkin reaction at high pressure [21] yields ΔV^* +3·3 c.c./mole, and this low value has been held to demonstrate close similarity between the quaternary salt and the transition state. However ΔV^* was calculated from the ratio k_{3000}/k_1, and the first-order rate constant depended on the initial concentration so that the significance of the result is doubtful.

ΔV^*, *the Volume of Activation.*—Values of ΔV^* at 1 atm. for the reactions of Table 1 are given in Table 2, together with those for other Menschutkin reactions for which rate constants at 1000 atm. or below are available. ΔV^* is obtainable from the curves, drawn in the way described, with an accuracy of 1—2 c.c./mole. The largest $-\Delta V^*$ is 47 c.c./mole

[15] Gonikberg and Povkh, *Zhur. fiz. Khim.*, 1949, **23**, 383.
[16] Perrin, *Trans. Faraday Soc.*, 1938, **34**, 150.
[17] Hamann, *Austral. J. Chem.*, 1956, **9**, 533.
[18] Gonikberg and Zhulin, *Austral. J. Chem.*, 1958, **11**, 285.
[19] Syrkin and Gubareva, *Acta Physicochim. U.R.S.S.*, 1938, **8**, 236.
[20] Weale, *Discuss. Faraday Soc.*, 1956, **22**, 122.
[21] Williams, Perrin, and Gibson, *Proc. Roy. Soc.*, 1936, *A*, **154**, 684.

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for the reaction between dimethylaniline and isopropyl iodide (Brower [22] has reported volume changes up to −64 c.c./mole for the reactions of bromonaphthalenes and bromoquinolines with an excess of piperidine at 150°). ΔV^* decreases with rising pressure and at 2500 atm. is usually only about half its initial value. The decrease is related to the

TABLE 2. *Volumes and entropies of activation at* 1 *atm.*

Reaction	Solvent	Temp.	$-\Delta V^*$ (c.c./mole) exp.	G. & K.	$-\Delta S^*$ (e.u.)
$NPhMe_2$ + MeI	MeOH	52·5°	26	15	30·4
$NPhMe_2$ + EtI	,,	,,	34	25	29·0
$NPhMe_2$ + EtI	$PhNO_2$	,,	20	25	41·9
$NPhMe_2$ + n-BuI	MeOH	,,	34	25	28·5
$NPhMe_2$ + i-PrI	,,	,,	47	40	20·4
Quinoline + EtI	,,	,,	20	13	19·7
$Ph{\cdot}CH_2{\cdot}NMe_2$ + EtI	,,	,,	27	13	22·9
NPr^n_3 + EtI	,,	,,	24	13	20·2
o-$C_6H_4Me{\cdot}NMe_2$ + MeI (2)	,,	50·0	24	18	18·9
o-$C_6H_4Me{\cdot}NMe_2$ + MeI (20)	$COMe_2$	,,	—	—	40·0
Pyridine + EtI (16, 18)	,,	40·0	30	10	35·3

increased initial density of the system, which brings the initial state closer in volume to the less compressible transition state, and it is significant that the variation of ΔV^* with the specific volume of the solvent is approximately linear in the experimental pressure range.

While our work was in progress Gonikberg and Kitaigorodskii [23] published calculations of ΔV^* for some Menschutkin reactions which take account only of volume changes considered to occur as a result of the close approach of the reactant molecules, solvation effects being ignored. An N–C distance of 1·5 Å in the transition state is assumed and the volume decrease due to the approach of these two atoms is calculated as the volume of interpenetration of two spheres of radii 1·6 Å and 1·8 Å, which corresponds to 4·7 c.c./mole. The alkyl groups of the iodide are assumed to occupy a plane perpendicular to the N–C axis and the alkyl groups of the amine to be disposed pyramidally at angles of 108°. If the amine contains a phenyl group the N–phenyl bond is parallel to the plane of the alkyl groups, and if it contains a pyridine ring this is perpendicular to the plane. Some non-bonded atoms or groups are found to approach closer than the sum of their van der Waals radii and each of these " volumes of compression " is also calculated from the volume of interpenetration of the spheres. Gonikberg and Kitaigorodskii take ΔV^* to be the sum of the individual volumes of compression. In Table 2 we include values of ΔV^* calculated by this method (but with a correction of +4 c.c./mole to allow for partial separation of the iodine atom).

The " G. & K." volumes vary in the same way and to a similar extent as ΔV^* for most of the reactions in methanol but, if the calculations are even approximately correct, only a small part of ΔV^* arises from solvation, and the difference between the solvation of the transition state and the quaternary salt is considerably greater than that indicated by the difference between ΔV^* and ΔV_s. This seems an improbable conclusion, and the theory also does not account for the large difference in ΔV^* for the same reaction ($NPhMe_2$ + EtI) in methanol and in nitrobenzene. A further objection is that if the main effect of pressure is to overcome repulsions between non-bonded atoms arising in the transition state it should reduce the activation energy considerably (which is generally not observed) instead of changing principally the entropy of activation.

Steric repulsions between non-bonded atoms certainly occur in reactions involving the more complicated amines and iodides, and contribute, together with electron-displacement and solvation, to the differences in activation energies among Menschutkin reactions. In some cases steric hindrance is responsible for the absence of any appreciable reaction. We did not observe formation of a quaternary salt from *NN*-dimethyl-*o*-toluidine and

[22] Brower, *J. Amer. Chem. Soc.*, 1958, **80**, 2105.
[23] Gonikberg and Kitaigorodskii, *Proc. Acad. Sci. U.S.S.R., Chem. Section*, 1958, **122**, 665.

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isopropyl iodide, and neither 2,5,*N*,*N*-tetramethyl- nor *o*-t-butyl-*NN*-dimethyl-aniline reacts with methyl iodide.[24] However, these non-bonded interactions are unlikely to give rise to the additive volume changes envisaged by Gonikberg and Kitaigorodskii. The variations of ΔV^* with molecular structure must be ascribed to other causes, and we consider that they reflect the influence of the structure and spatial distribution of substituent groups on the solvation of the transition state. This explanation is considered in greater detail in the following sections.

ΔS^*, *the Entropy of Activation.*—The entropies of activation for the reactions at 1 atm., calculated from the well-known equation:

$$k = (e\boldsymbol{k}T/\boldsymbol{h}) \exp (\Delta S^*/\boldsymbol{R}) \exp (-E/\boldsymbol{R}T)$$

are given in Table 2. Although it has been suggested [25] that a " cratic " correction may be made to ΔS^* to allow for a change in the number of moles of solute species we prefer to use the experimental values for comparative purposes. In methanol these vary by a factor of about 1·6, and in the reactions between dimethylaniline and the four alkyl iodides ΔS^* varies inversely with ΔV^*, so that the largest volume decrease corresponds to the lowest entropy change. These differences, which determine the effect of pressure on the rate constants, are attributed to differences in the solvation of the transition state. A model of the *NNN*-trimethylanilinium iodide transition state show that there are four exposed segments of the nitrogen atom to which a methanol-oxygen atom can approach closely, *i.e.*, to within about 1 Å. The incipient positive ion of this transition state can therefore be solvated by four fairly tightly bound solvent molecules, and it is reasonable to suppose that this situation will correspond to a rather high entropy of activation and to a considerable, but not exceptionally large, volume of activation. In the *N*-ethyl-*NN*-dimethyl transition state only two of the segmental faces of the nitrogen atom are as accessible as before. Development of the positive charge may therefore demand the binding of a greater number of more distant methanol molecules. This difference is considered to result in an increased volume change, because of the greater volume of the solvation shell, but in a smaller entropy decrease. Finally, in the *N*-isopropyl-*NN*-dimethyl transition state only one segment of the nitrogen atom remains easily accessible to a methanol molecule. This is expected to result in weak binding of a still larger number of solvent molecules, and this instance corresponds to the greatest ΔV^* and the lowest ΔS^*. Laidler [26] has suggested that weaker binding will be associated with larger values of the temperature coefficient of ΔV^* which can be evaluated from the entropies of activation since $\delta\Delta V^*/\delta T = -\delta\Delta S^*/\delta P$. In the reaction of dimethylaniline with methyl iodide the entropy change, $-\Delta S^*$, decreases by 6 e.u. between 1 and 2875 atm., while for the reactions with ethyl and butyl iodide the change is about 11 e.u., which supports this interpretation. For reaction with isopropyl iodide the difference $\Delta S^*_{2875} - \Delta S^*_1$ is, however, 4·8 e.u. Probably the suggested correlation is inapplicable when there are large variations between the binding of different solvent molecules.

In the reactions of quinoline, benzyldimethylamine, and tri-n-propylamine with ethyl iodide fewer than four methanol molecules can approach closely the nitrogen atom of the transition state. The entropy of activation is less than for dimethylaniline but the values of ΔV^* are very similar. No detailed comparison is possible as there may be appreciable differences in the interaction between methanol and the unactivated amines in the initial state.

The Effect of the Solvent on ΔV^* *and* ΔS^*.—There is not much systematic information about the variation of the pressure effect for the same reaction in different solvents. The reaction between pyridine and ethyl iodide is accelerated by increase of pressure almost equally [27] in acetone and in hexane at 2980 atm., but the acceleration of the reaction

[24] Brown and Grayson, *J. Amer. Chem. Soc.*, 1953, **75**, 20; Brown and Nelson, *ibid.*, p. 24.
[25] Burris and Laidler, *Trans. Faraday Soc.*, 1955, **51**, 1497.
[26] Laidler, *Discuss. Faraday Soc.*, 1956, **22**, 88.
[27] Gibson, Fawcett, and Perrin, *Proc. Roy. Soc.*, 1935, *A*, **150**, 233.

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between methyl iodide and *NN*-dimethyl-*o*-toluidine is about 30% greater in acetone than in methanol. An apparently general difference between acetone and methanol is that the effect of pressure on Menschutkin reactions in acetone is to increase both the A and the E factor, while in methanol parameter A is increased but E is usually little affected or is reduced.

There is a large difference between the pressure effect on the reaction of dimethylaniline and ethyl iodide in methanol and in nitrobenzene, which is one of the arguments against Gonikberg and Kitaigorodskii's hypothesis. ΔV^* is much smaller in nitrobenzene and its decrease with increasing pressure is less marked. The low value of ΔV^* is no doubt associated with the pronounced interaction between nitrobenzene and aromatic amines in solution,[28] and it is also probable that, because of their high polarity, fewer solvating molecules are required to reduce the free energy of activation. The smaller variation of ΔV^* may be attributable to the reduced compressibility of nitrobenzene compared with methanol.

The structures of methanol, acetone and nitrobenzene do not prevent close approach of the solvent-oxygen atom to the transition state nitrogen atom, but in other cases the solvent structure may increase the hindrance to solvation. This perhaps occurs to some extent in the reactions studied by Brower [22] with excess of piperidine as solvent. The bulkiness of transition-state and solvent configurations results in a larger, less strongly bound solvation shell, and a high volume of activation.

The authors are indebted to Mr. J. M. Stewart for data on the reaction in nitrobenzene, and one of them (A. P. H.) thanks the Edwards Trust and the C.S.I.R. of South Africa for financial assistance.

Department of Chemical Engineering and Chemical Technology,
Imperial College, S. Kensington,
London, S.W.7. [*Received, July 18th*, 1960.]

[28] Gibson and Loeffler, *J. Amer. Chem. Soc.*, 1940, **62**, 1324.

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28. *Akuamma Alkaloids. Part II.*[1] *The Structure of Akuammicine.*

By P. N. Edwards and G. F. Smith.

Akuammicine is shown to have structure (I) by conversion into the amino-ester (V), prepared from the Wieland–Gumlich aldehyde (II).

In a previous communication [1] we described a degradation of akuammicine which led to the proposal of a partial structure compatible with (I), the structure suggested for the alkaloid by Sir Robert Robinson and Aghoramurthy.[2] Since the prospects of a complete proof of structure by a continuation of the above degradative approach did not appear to be promising, we turned our attention to conversion of akuammicine into a compound which might in its turn be prepared from strychnine.

Akuammicine is quantitatively reduced by zinc and methanolic sulphuric acid to a dihydro-derivative, $C_{20}H_{24}O_2N_2$, in which the akuammicine ultraviolet absorption, with a long-wavelength maximum at 329 mμ, has been replaced by absorption characteristic of an indoline base, and in which the ester-carbonyl infrared absorption has moved to the usual region around 1730 cm.$^{-1}$. This means that the product is, on the basis of structure (I), 2,16-dihydroakuammicine. The reduction thus proceeds in a manner completely analogous with that of fluorocurarine.[3] The dihydro-base takes up one mol. of hydrogen

[1] Smith and Wróbel, *J.*, 1960, 792.
[2] Robinson and Aghoramurthy, *Tetrahedron*, 1957, **1**, 172.
[3] Von Philipsborn, Bernauer, Schmid, and Karrer, *Helv. Chim. Acta*, 1959, **42**, 461.

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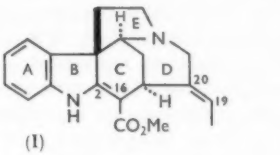
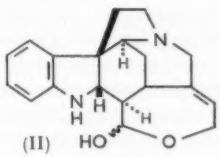
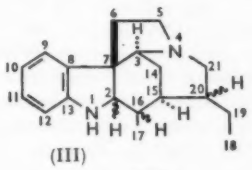
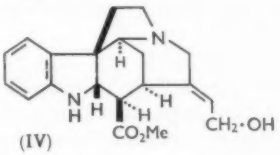
in the presence of Adams catalyst to give 2,16,19,20-tetrahydroakuammicine, $C_{20}H_{26}O_2N_2$. The same tetrahydro-base is obtained by reduction of 19,20-dihydroakuammicine with zinc and methanolic sulphuric acid.

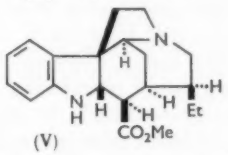
Treatment of the tetrahydroakuammicine with sodium methoxide and magnesium methoxide in methanol at 100° results in epimerisation of the methoxycarbonyl group with the formation of isotetrahydroakuammicine.

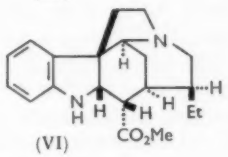

(I)


(II)


(III)


(IV)


(V)


(VI)

The well-known strychnine degradation product, the Wieland–Gumlich aldehyde [4] (II), was used as the starting point for a synthesis of isotetrahydroakuammicine. Attempts to oxidise the lactol grouping in the *N*-acetyl derivative of (II), diaboline,[5] with manganese dioxide in chloroform or benzene,[6] or with aqueous chromic acid at 100°, failed. An indirect method, however, was successful. The oxime [4] of the Wieland–Gumlich aldehyde was dehydrated by acetic anhydride in pyridine and from the mixed products chromatography on alumina gave a sharp non-crystalline fraction (about 65%) whose infrared and ultraviolet spectra showed it to consist largely of the expected 18-acetoxy-1-acetyl-16-cyano-17-nor-2β,16α-cur-19-ene.* Alkaline hydrolysis of this product, followed by esterification with methanolic hydrochloric acid and chromatography on alumina, gave crystalline methyl 18-hydroxy-2β,16α-cur-19-en-17-oate (IV) in about 30% yield (based on the oxime). The stereochemistry of this product (IV) was fixed by reduction with lithium aluminium hydride which gave 2β,16α-cur-19-ene-17,18-diol (the Wieland-Gumlich diol [8]). The methoxycarbonyl group of the curenoate (IV) was not epimerisable. Attempts to remove the allylic hydroxyl group by hydrogenolysis [7] of the corresponding bromide with zinc and acetic acid failed; on the other hand hydrogenolysis of the ester (IV) with hydrogen and Adams catalyst in methanolic perchloric acid resulted in the uptake of 1·6 mol. of hydrogen and the formation of methyl 2β,16α,20α-curan-17-oate, $C_{20}H_{26}O_2N_2$, identical with isotetrahydroakuammicine. This base must have structure (V); hence tetrahydroakuammicine has structure (VI) (methyl 2β,16β,20α-curanoate), and akuammicine has structure (I), with only the stereochemistry of the ethylidene double bond to be established.

It is of interest to speculate on the stereochemistry of the reduction of the 2,16-double bond in akuammicine by zinc and sulphuric acid. The first step in the reaction must

* The nomenclature used in this paper is based on preliminary proposals received from Professor M.-M. Janot and Dr. J. Le Men (personal communication, July 13th, 1960). Full details of a comprehensive system of nomenclature for β-indole alkaloids will be published by Professor Janot and Dr. Le Men. The curan system is formulated as (III), without specification of stereochemistry at positions 2, 16, and 20. The numbering follows that of Bernauer *et al.*[7]

[4] Wieland and Karizo, *Annalen*, 1933, **506**, 60; Wieland and Gumlich, *ibid.*, 1932, **494**, 191.
[5] Battersby and Hodson, *Proc. Chem. Soc.*, 1959, 126.
[6] Highet and Wildman, *J. Amer. Chem. Soc.*, 1955, **77**, 4399.
[7] Bernauer, Berlage, von Philipsborn, Schmid, and Karrer, *Helv. Chim. Acta*, 1958, **41**, 2293.
[8] Anet and Robinson, *J.*, 1955, 2253.

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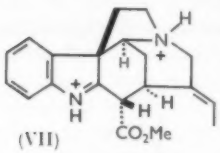
almost certainly be protonation [9] of $C_{(16)}$ to give the immonium ion (VII). The proton adds to the β-face in order to allow the methoxycarbonyl group to take up the more stable equatorial orientation, ring C being in the boat conformation. Reduction of the $C_{(2)}$ then proceeds by addition of hydrogen again to the β-face, to give an ester (VI) in which the B/C ring junction is the more stable *cis*-form and rings C and D have chair conformations. This forces the methoxycarbonyl group into an axial orientation. Epimerisation of tetrahydroakuammicine to the isomeric base (IV) is then readily understood, for it involves a change of orientation of the methoxycarbonyl group from axial to equatorial. The axial orientation of the ester group in tetrahydroakuammicine brings the ester-carbonyl group within hydrogen-bonding distance of the NH group, which accounts for the twinning (1746, 1726 cm.$^{-1}$) of the carbonyl band in the infrared spectrum of this base. In the iso-base (V) the ester group is well out of reach of the *N*-hydrogen atom, and the infrared carbonyl absorption is a single band at 1732 cm.$^{-1}$.



(VII)

The preparation of Wieland-Gumlich aldehyde has, in our hands and also in the experience of another research group,[10] consistently given a yield (~20%) much lower than that (33%) quoted by earlier workers.[8] In our last two preparations we isolated ~5% of a chloroform- and water-soluble, ether-insoluble by-product which has been shown, by its ready formation from the Wieland-Gumlich aldehyde and bromochloromethane-free chloroform [11] at the boiling point, to be the αα-dichloromethochloride of this base. It follows that the yield of Wieland–Gumlich aldehyde would be appreciably raised by avoiding the use of chloroform during the working up of the reaction mixture.

[*Note, added June 22nd*, 1960.] Methyl 2β,16β,20α-curan-17-oate (VI) was reduced by lithium aluminium hydride to 2β,16β,20α-curan-17-ol, isolated as the crystalline methiodide. Through the courtesy of Professor M.-M. Janot, this methiodide has been shown to be identical with geissoschizoline methiodide, which confirms the structure proposed by Puisieux *et al.*[12] for this geissospermine hydrolysis product. Professor Janot informs us that he has also independently established the structure of geissoschizoline.

Experimental

Methyl 2β,16β-*Cur*-19-*en*-17-*oate* (2,16-*Dihydroakuammicine*).—A solution of akuammicine (220 mg.) in 10% absolute methanolic sulphuric acid (100 c.c.) was treated with zinc dust (30 g.), and the mixture heated under reflux for 30 min. with vigorous shaking. The filtered solution was evaporated to small bulk *in vacuo* and treated with water (50 c.c.) and then with sodium carbonate solution to permanent turbidity. Aqueous ammonia (20 c.c.; *d* 0·880) was then added and the whole immediately extracted with ether (5 × 30 c.c.). The ether extract yielded *methyl* 2β,16β-*cur*-19-*en*-17-*oate* (198 mg.) which, after two crystallisations from light petroleum (b. p. 80—100°), formed prisms, m. p. 143—145° (Found: C, 74·1; H, 7·35. $C_{20}H_{24}N_2O_2$ requires C, 74·05; H, 7·45%), $\lambda_{max.}$ 299, 246 mμ (ε 3900, 8700 in MeOH), $\nu_{max.}$ (in CCl_4), 3400w, 1747s, 1729s cm.$^{-1}$.

Methyl 2β,16β,20α-*Curan*-17-*oate* (*Tetrahydroakuammicine*) (VI).—(i) The above base (200 mg.) was hydrogenated in methanolic 10% acetic acid (25 c.c.) in the presence of Adams catalyst (59 mg.). The hydrogen uptake ceased after 30 min (1·1 mol. taken up). Working up the solution for basic material yielded the *curanoate* (189 mg.) which, after two crystallisations from light petroleum, was obtained as needles, m. p. 135—137° (Found: C, 73·55; H, 8·0. $C_{20}H_{26}N_2O_2$ requires C, 73·6; H, 8·05%), $\lambda_{max.}$ 299, 246 mμ (ε 3600, 8300 in MeOH), $\nu_{max.}$ (in CCl_4) 3400w, 1746s, 1726s cm.$^{-1}$.

(ii) 19,20-Dihydroakuammicine (73 mg.) was reduced with zinc and methanolic sulphuric acid under the conditions described above for the reduction of akuammicine. The product formed needles, m. p. and mixed m. p. 134·5—136·5° (65 mg.).

[9] Fritz, *Chem. Ber.*, 1959, **92**, 1809.
[10] Battersby, personal communication.
[11] Williams, *Chem. and Ind.*, 1960, 900.
[12] Puisieux, Goutarel, Janot, Le Men, and Le Hir, *Compt. rend.*, 1960, **250**, 1285.

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Methyl 18-*Hydroxy*-2β,16α-*cur*-19-*en*-17-*oate* (IV).—A mixture of the Wieland–Gumlich oxime [4] (2·88 g.), acetic anhydride (30 c.c.), and pyridine (5 c.c.) was heated at 100° for 90 min., the solvent removed *in vacuo*, and the residue partitioned between 20% aqueous sodium carbonate (25 c.c.) and ethyl acetate (15 c.c.). The aqueous phase was extracted further with ethyl acetate (2 × 15 c.c.), the combined extracts were evaporated, and the residue (3·21 g.) was adsorbed on alumina (50 g.) and eluted with chloroform (500 c.c.). The eluate (2·42 g.) did not crystallise [$\nu_{max.}$ (in CCl_4) 3630w, 2260vw, 1748s, 1680s cm.$^{-1}$]. A solution of this product in ethanol (50 c.c.) was refluxed with one of barium hydroxide (9·5 g.) in hot water (100 c.c.) under nitrogen for 16 hr. Sulphuric acid (3·0 g.) was then added, barium sulphate filtered off, and the solution evaporated to dryness. The residue was refluxed with methanolic 5% hydrochloric acid (150 c.c.) for 5 hr., and again evaporated to dryness. The residue was treated with 10% aqueous sodium carbonate (100 c.c.) and the whole extracted with ethyl acetate (4 × 25 c.c.). The dried combined extracts yielded crude *methyl* 18-*hydroxy*-2β,16α-*cur*-19-*en*-17-*oate* (1·32 g.) which after three crystallisations from methanol formed needles, m. p. 152—154·5° (sintering at 110°) (Found, in material dried at room temperature *in vacuo*: C, 68·1; H, 7·4. $C_{20}H_{24}N_2O_3,CH_3OH$ requires C, 67·7; H, 7·6%). The solvent-free *ester* crystallises from benzene as needles, m. p. 154—156° (Found: C, 70·7; H, 7·1. $C_{20}H_{24}N_2O_3$ requires C, 70·55; H, 7·1%), $\lambda_{max.}$ 301, 246 mμ (ε 2600, 6200 in MeOH), $\nu_{max.}$ (in CCl_4) 3550w, 3400w, 1732s cm.$^{-1}$.

2β,16α-*Cur*-19-*ene*-17,18-*diol* (*Wieland–Gumlich Diol*).—The preceding ester (56 mg.) in benzene (5 c.c.) was treated with excess of lithium aluminium hydride in ether (150 c.c.), and the mixture refluxed for 24 hr. 20% Aqueous sodium hydroxide (50 c.c.) was added, the whole shaken, and the ether layer separated. The aqueous phase was extracted with chloroform (2 × 50 c.c.). The combined, dried ether and chloroform extracts yielded a gum (50·4 mg.) which crystallised (45 mg.) from benzene–methanol. Two more crystallisations yielded the pure diol as prisms, m. p. 245—248° with some distillation on to the cover slip from 240°. This m. p. was not depressed by the product (identical m. p.) of reduction of the Wieland–Gumlich aldehyde [7] by lithium aluminium hydride. The infrared spectra (Nujol mull) were identical.

Methyl 2β,16α,20α-*Curanoate* (V).—(i) The ester (IV) (351 mg.) in absolute methanol (50 c.c.) containing aqueous perchloric acid (1 c.c.; 60% w/v) was hydrogenated in the presence of Adams catalyst for 3 hr., by which time the rate of hydrogen uptake had slowed very considerably and 1·6 mol. had been absorbed. The basic product (343 mg.) was passed through neutral alumina (10 g.) by means of ether (100 c.c.). The eluate (207 mg.), crystallised three times from light petroleum, gave the pure *ester* (V) as needles, m. p. 152—153° (165 mg.). Slow crystallisation from light petroleum at room temperature gives a polymorph (prisms), m. p. 129—131° (Found: C, 73·2; H, 7·85; OMe, 9·5. $C_{20}H_{26}N_2O_2$ requires C, 73·6; H, 8·05; 1OMe, 9·5%), $\lambda_{max.}$ 299, 245 mμ (ε 3000, 7200 in MeOH), $\nu_{max.}$ (in CCl_4) 3430w, 1732s cm.$^{-1}$, $[\alpha]_D^{22}$ −139° (*c* 1·1 in MeOH).

(ii) A solution of tetrahydroakuammicine (VI) (47 mg.) in methanol (1 c.c.), in which magnesium (25 mg.) and sodium (10 mg.) had been dissolved, was heated in an evacuated tube at 100° for 3 hr., then treated with water (10 c.c.) and immediately extracted with ether (3 × 20 c.c.). The dried ether extracts yielded a product (47 mg.) which after three crystallisations from light petroleum formed needles, m. p. 151—152·5°, identical (including formation of the polymorph), with the ester (V) obtained as above.

Wieland–Gumlich Aldehyde (II) *and its Dichloromethochloride*.—The preparation was carried out with 112 g. of strychnine, according to Anet and Robinson's directions [8] up to the final chloroform extraction of the total product. Material from this extract was crystallised from chloroform: the first crop consisted of needles which did not melt but gradually decomposed above 200° (3·5 g.); the second crop consisted of impure Wieland–Gumlich aldehyde which on recrystallisation from methanol–acetone gave a product, m. p. 200—215° (10·1 g.). The combined chloroform and methanol–acetone mother-liquors were chromatographed on neutral alumina containing 10% of water: benzene–chloroform (3 : 2) eluted more impure aldehyde (7·0 g.); chloroform–methanol (9 : 1) eluted the quaternary salt, decomp. >200° (1·5 g.). The combined aldehyde fractions were recrystallised twice from methanol–acetone to give the pure product, m. p. 212·5—215° (12 g., 20%).

The combined quaternary salt fractions (5 g., 5%) were recrystallised several times from methanol, giving the *aldehyde dichloromethochloride* as needles, decomp. >200° (Found, in

material dried at room temperature *in vacuo*: C, 51·5, 51·05; H, 5·95, 6·2. $C_{20}H_{23}Cl_3N_2O_3,2H_2O$ requires C, 51·55; H, 5·8%), $\lambda_{max.}$ 293, 239 mμ (ε 2900, 7900 in MeOH), soluble in water.

Interaction of Wieland–Gumlich aldehyde and boiling bromochloromethane-free chloroform [11] gave the same compound.

Acknowledgment is made to the D.S.I.R. for a Maintenance Award (to P. N. E.) and to the Tropical Products Council for *Picralima* seeds.

THE UNIVERSITY, MANCHESTER. [*Received, April 19th*, 1960.]

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29. *Photochromism in Some Spiropyrans. Part III.*[1] *The Extent of Phototransformation.*

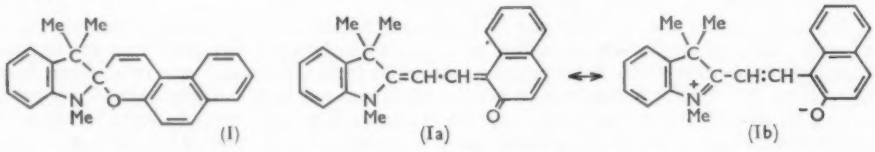
By RAHEL HEILIGMAN-RIM, (the late) YEHUDA HIRSHBERG, and ERNST FISCHER.

Photochromic spiropyrans were observed to have a narrow absorption band at about 245 mμ, characteristic for the colourless modification of these compounds. This band diminishes when the spiropyrans are converted by ultraviolet irradiation into the corresponding coloured dimethinmerocyanines, and reappears when the latter are reconverted into the spiropyrans. The attenuation of this band can therefore be used to estimate the extent of phototransformation, which was thus found to vary between 50% and 100%. Solutions of some compounds commonly thought to be dimethinmerocyanine dyes also show the above absorption band, and probably consist of equilibrium mixtures of the merocyanines and the corresponding spiropyrans.

PARTS I and II of this series and related publications [1-5] gave a qualitative description of the phenomenon of photochromism in thermochromic and related spiropyrans. This phenomenon consists (*a*) of the transformation of these colourless compounds into coloured modifications when their solutions are irradiated with ultraviolet light at low temperatures and (*b*) of the reverse process which takes place when the temperature is raised and also, in some cases, at low temperature as a result of irradiation with visible light:

$$\text{Colourless modification} \underset{h\nu_2}{\overset{h\nu_1}{\rightleftharpoons}} \text{Coloured modification} \quad (\nu_1 > \nu_2)$$

It should be recalled that the phototransformations all result in attainment of photoequilibria and not thermodynamic equilibria. The latter are generally almost completely in favour of the spiropyran, and their establishment is prevented at sufficiently low temperatures only by the potential barrier of 15—20 kcal./mole which has to be passed when the merocyanine is converted into the spiropyran.[4] With the spiropyrans described in the present paper, thermodynamic equilibrium is established rapidly at temperatures above about −50°.



(I) (Ia) (Ib)

When a (colourless) solution of, *e.g.*, the spiran (I) is irradiated with ultraviolet light, at temperatures below about −90°, it becomes intensely violet-red.[2] This was explained [2]

[1] Part II, Hirshberg and Fischer, *J.*, 1954, 3129.
[2] Fischer and Hirshberg, *J.*, 1952, 4522.
[3] Hirshberg, Frei, and Fischer, *J.*, 1953, 2184.
[4] Hirshberg and Fischer, *J.*, 1954, 297 (Part I).
[5] Hirshberg, *J. Amer. Chem. Soc.*, 1956, **78**, 2304.

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as being due to transformation into an isomeric dimethinmerocyanine-like modification which is actually a resonance hybrid of (Ia) and (Ib), in analogy with the structure suggested by several authors [9] for the thermochromic coloured modification of (I).

The colourless modification is re-formed from the coloured one either spontaneously,[2] when the solution is heated above about −50°, or by irradiation with visible light at the low temperature at which coloration took place.[3]

It was also shown that, whenever such a compound is convertible into both thermochromic and photochromic modifications, these two are identical and that, as observed in the bianthronyl series investigated earlier,[6,7] photochromism is also exhibited by some non-thermochromic spiropyrans.

Since then, greatly improved techniques,[8] including rigorous exclusion of air and hydroxylic contaminants from solutions in non-polar solvents, and information from related fields of research, have made possible more accurate and quantitative experimental work, and more insight can now be gained into the nature of the coloured isomers, the mechanism of the phototransformation, and the extent to which it takes place. These three aspects of the phenomenon form the subjects of the present and the two following parts of this series.*

Figs. 1a and 1c show the effect of progressive ultraviolet irradiation on solutions of the spiran (I) at two concentrations, namely, gradual appearance of the visible absorption bands, accompanied by pronounced changes in the ultraviolet region, the most marked being the gradual diminution of the sharp band at 244 mμ. Several well-defined isosbestic points are observed in the region in which both modifications absorb (Fig. 1c).

Ultraviolet irradiation of several other photochromic spiropyrans [1,4] (II)—(IX) resulted in somewhat similar spectral changes. Here too the most prominent change was diminution of a narrow band in the vicinity of 245 mμ, this band being common to the colourless modification of all the compounds. The results are summarized in Fig. 2, whereas details about the wavelength and the extinction coefficient of this absorption band are given in Table 1.

It is seen that for all naphthopyrans [(I)—(V)] the band in question is similar in shape and intensity and in the region of 244 ± 5 mμ. It probably corresponds to the ^1B_b transition, as defined by Platt.[10a] † For the benzopyran derivatives [(VI)—(IX)] the band is less intense and of a different shape and wavelength. It may correspond to the transition denoted by Platt as ^1L_a. The left-hand component (indoline, acridine, benzopyran) seems to have little effect on the band, which thus appears to characterize the closed, spiropyran structure given in the formulæ. The extent to which this band diminishes as a result of ultraviolet irradiation thus affords a means of estimating the degree of conversion of the spiropyrans into their coloured modifications analogous to (Ia) ⟷ (Ib). In order to carry out such an estimation, an assumption must be made regarding the extinction coefficient of the coloured modification at the wavelength of the above band. There is no exact basis for any such assumption. However, the lower limit of the coefficient is obviously zero, giving a lower limit for the calculated degree of conversion into the coloured

* For preliminary accounts see *Bull. Res. Council Israel*, 1958, **7**, *A*, 226; 1959, **8**, *A*, 151, 152.

† The ultraviolet spectra of the naphthopyrans closely resemble that of phenanthrene, which has absorption bands at 353, 303, and 252 mμ.[10b,c]

[6] Hirshberg, *Compt. rend.*, 1950, **231**, 903.

[7] Hirshberg and Fischer, *J.*, 1953, 629.

[8] Hirshberg and Fischer, *Rev. Sci. Instr.*, 1959, **30**, 197.

[9] (*a*) Dilthey and Wubken, *J. prakt. Chemie*, 1926, **114**, 179; (*b*) Dickinson and Heilbron, *J.*, 1927, 1699; (*c*) Wizinger and Wenning, *Helv. Chim. Acta*, 1940, **23**, 247; (*d*) Koelsch, *J. Org. Chem.*, 1951, **16**, 1362; (*e*) Knott, *J.*, 1951, 3038; (*f*) cf. also Chaudé's exhaustive study (Thèse, "Étude spectrophotometrique de l'isomerisation de divers spiranes thermochromes," edition de la Revue d'Optique, Paris, 1954).

[10] (*a*) Platt, *J. Chem. Phys.*, 1949, **17**, 484; (*b*) Klevens and Platt, *ibid.*, p. 470; (*c*) Klevens and Platt, "Survey of Vacuum Ultraviolet Spectra of Organic Compounds in Solution," Technical Report, Lab. of Molecular Structure and Spectra, University of Chicago, 1953—54.

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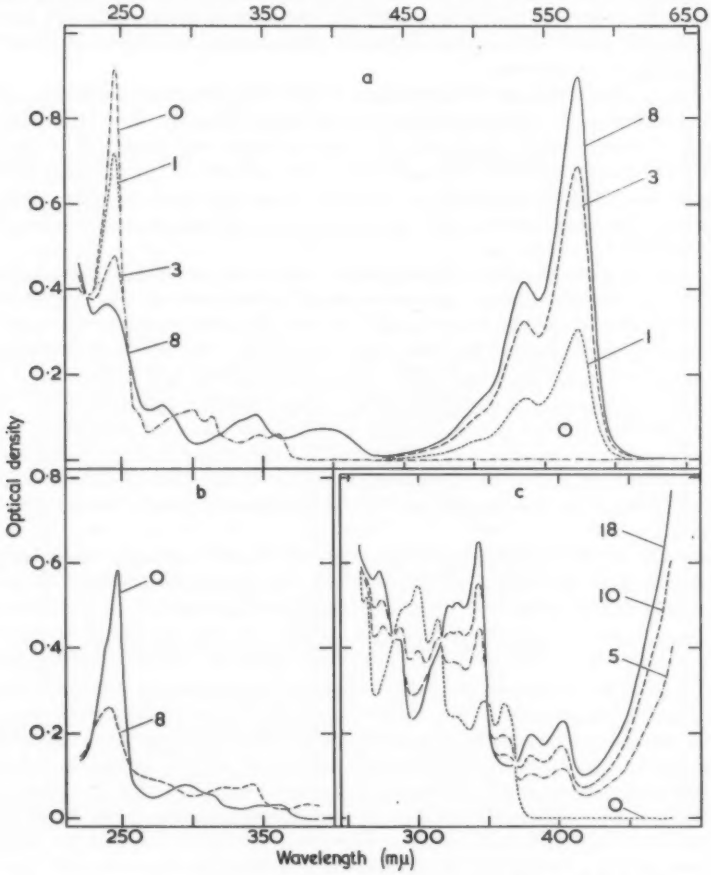
form, whereas the upper limit of the degree of this conversion is of course unity (*i.e.*, complete conversion). As an example, for compound (I) in Fig. 1a, the optical density of the band at 244 mμ is reduced by irradiation from 0·94 to 0·37. This then corresponds to

FIG. 1. *Spectra of solutions of spiran* (I) *before and after progressive irradiation with ultraviolet light at* 365 mμ. *Numbers on the curves denote time of irradiation, in minutes. In ethanol–methanol,* (a) 9×10^{-6}M, (c) 45×10^{-6}M. (b) *In methylcyclohexane–isopentane,* 5×10^{-6}M.



a content, after irradiation, of between ($100 \times 0{\cdot}37/0{\cdot}94 =$) 39% and 0% of spiropyran, or a degree of photoconversion into the coloured form of between 61% and 100%. The

TABLE 1. *" Spiropyran " bands for various compounds in alcoholic solution.*

Compound	Peak wavelength (mμ)	Molar extinction coeff. (10^{-3} ε)	Compound	Peak wavelength (mμ)	Molar extinction coeff. (10^{-3} ε)	Compound	Peak wavelength (mμ)	Molar extinction coeff. (10^{-3} ε)
(I)	244	78	(IV)	248	73	(VII)	225	16
(II) *	244	140	(V)	249	63	(VIII)	245 (283)	15 †
(III)	239	74	(VI)	229 (291)	31 (7)	(IX)	226	25 †

* This compound contains two naphthopyran systems, and its " spiropyran " band is therefore about twice as high as those for the other naphthopyrans. † For technical reasons these values are only approximations.

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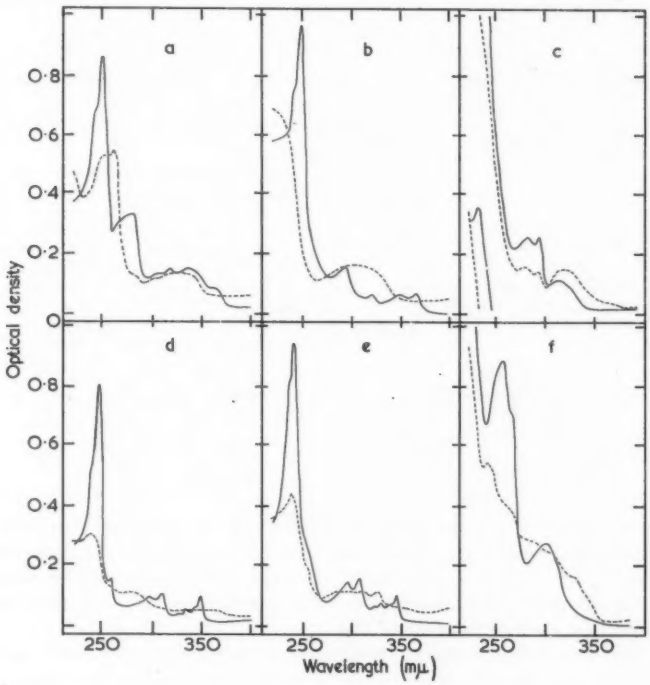
FIG. 2. *Ultraviolet absorption spectra of some spiropyrans, before (full curves) and after (broken curves) irradiation with ultraviolet light. All solutions, except* d, *in ethanol–methanol.* (a) *Compound* (V) (1×10^{-5}M) *at* $-120°$, *irradn. at* 365 mμ; (b) *compound* (IV) (1×10^{-5}M) *at* $-120°$, *irradn. at* 365 mμ; (c) *compound* (VI) ($3{\cdot}5 \times 10^{-5}$M) *at* $-100°$, *irradn. at* 365 + 313 + 303 mμ; (d) *compound* (II) ($0{\cdot}6 \times 10^{-5}$M) *in methylcyclohexane, at* $-120°$, *irradn. at* 313 + 303 mμ; (e) *compound* (III) (1×10^{-5}M) *at* $-120°$, *irradn. at* 365 + 313 + 303 mμ; (f) *compound* (VII) (4×10^{-5}M) *at* $-80°$, *irradn. at* 365 + 313 + 303 mμ.



minimum values based on results of similar calculations, based on the data in Figs. 1 and 2, are summarized in the second column of Table 2.

TABLE 2. *Degrees of photoconversion of some spiropyrans into the coloured modifications, and molar extinction coefficients of these modifications.* (*Solutions in ethanol–methanol.*)

Compound	Conversion (%) into coloured modification		Main visible absorption band of coloured modification		
	Minimal	Probable	(mμ)	($10^{-3}\varepsilon$) max.[b]	($10^{-3}\varepsilon$) probable
(I)	62	88	573	120	85
(I)[a]	60	80	525	85	65
(II)	75	90	645	—	—
(II)[a]	65	90	600	32	25
(III)	55	70	568	62	47
(IV)	75	95	520	37	27
(V)	38	80	696	87	40
(VI)[c]	45	65	590	20	13
(VII)	55	90	622	18	10

[a] Solution in isopentane–methylcyclohexane. [b] Corresponding to minimal degree of conversion into the coloured modification. [c] From the absorption band at 291 mμ.

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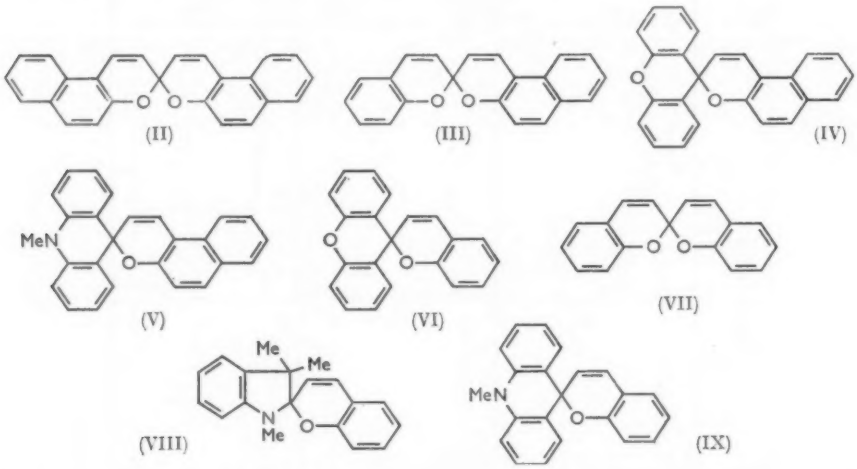
Inspection of Figs. 1 and 2 shows that the actual degrees of conversion are probably somewhere between the minimal percentages given and 100%. If in each case a " reasonable " assumption is made regarding the shape of the coloured modification's absorption curve, a " probable " degree of conversion can be calculated from such a curve and the two experimental curves. The results are given in the third column of Table 2. Both the minimal and the " probable " values for the degrees of conversion may serve to assess



the molar extinction of the main absorption bands of the coloured forms in the visible region. Approximate values for these coefficients are given in the last two columns. The data collected in Table 2 appear to be the first direct experimental estimate of the degree of photoconversion of photochromic compounds into their coloured modification, and of the extinction coefficient of the latter.

An earlier paper from this Institute [11] pointed out the similarity between some dimethinmerocyanine dyes and the thermochromic coloured modification of some spiropyrans. It was suggested at that time that, *e.g.*, compound (X) might actually exist in solution as a mixture of the open merocyanine-like form (Xa) and the closed, spiropyran form (Xb).

This suggestion was challenged by Knott,[9e] but its correctness has now been proved by the method outlined in the present paper. The two dyes [12] (X) and (XI), whose structural formulæ in their (assumed) closed form (b) closely resemble that of spiropyran (I), were investigated. Fig. 3 shows the spectra of these two in decalin (full curves) and alcohol (broken curves), together with the spectra of spiropyrans (I) and (V) in their colourless (full curves) and coloured (broken curves) modifications. Comparison of Figs. 3a, 3b, and 3c shows a striking resemblance between the ultraviolet spectra of the colourless spiropyrans and those of the decalin solutions of compounds (X) and (XI), and also between the visible spectra of the alcoholic solutions of the dyes and those of the photochromic coloured modifications. The predominance of the spiropyran form is particularly striking in decalin solutions of dye (XI) (Fig. 3b), which are actually thermochromic. In alcoholic solutions of the same compound the open form is seen to predominate. This solvent effect on the thermal equilibrium between the two forms is similar to that observed with thermochromic spiropyrans.[4,5] Attempts to change the ratio between the two forms by irradiation at low temperatures have hitherto failed with both dyes.

If acid is added at room temperature to alcoholic solutions of those spiropyrans which

[11] Bergmann, Weizmann, and Fischer, *J. Amer. Chem. Soc.*, 1950, **72**, 5009.
[12] Hirshberg, Knott, and Fischer, *J.*, 1955, 3313.

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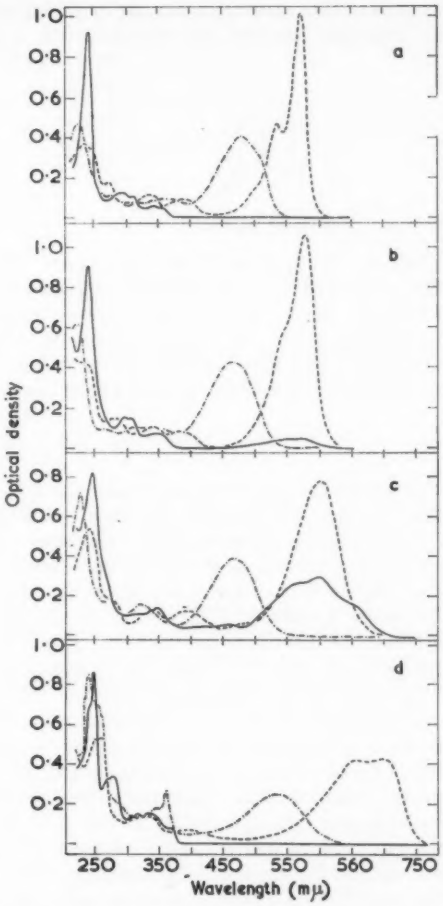
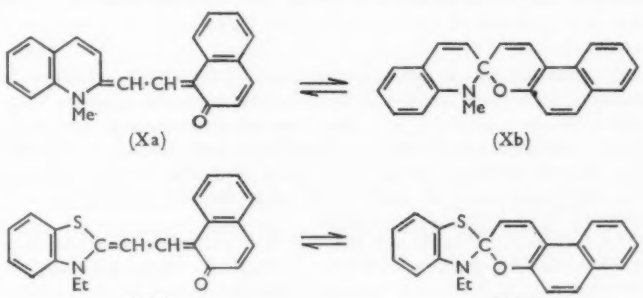


FIG. 3. *Absorption spectra of spiropyrans and merocyanines. Full curves, spiropyrans* (I) *and* (V) *in ethanol before irradiation, merocyanines* (X) *and* (XI) *in decalin; broken curves, same spiropyrans after ultraviolet irradiation, merocyanines in ethanol; dashed-dot curves, all compounds in ethanol at 25° after addition of excess of* HCl [600 *equiv. for* (I), 2 *equiv. for* (X), 10 *equiv. for* (XI), 60 *equiv. for* (V)]. (a) *Compound* (I), $0{\cdot}9 \times 10^{-5}$M, −100°; (b) *compound* (XI), $1{\cdot}5 \times 10^{-5}$M, +25°; (c) *compound* (X), *saturated solution in decalin,* $1{\cdot}6 \times 10^{-5}$M *in propanol,* +25°; (d) *compound* (V), 1×10^{-5}M, −120°.

are derived from acridine or indoline [(I), (V), (VIII), (IX)], they are converted into salts of the open merocyanine-like form,[5,9f] presumably by way of the free merocyanine base which exists in thermal equilibrium with the spiropyran form in all thermochromic compounds at or beyond room temperature.[9] Thus, for example, compound (I) is transformed,



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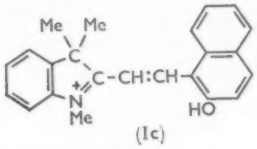
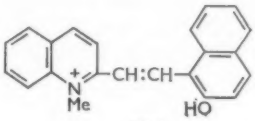
by way of (Ia) ⟷ (Ib), into (Ic). In the presence of excess of acid (about 600 equivalents of hydrogen chloride) the equilibrium is shifted completely in favour of form (Ic), thus



(Ic)



(Xc)

affording another path to the " open " structure, in addition to the photochromism described above. The dash-dot curves in Figs. 3a and 3d show the spectral changes involved. Here too the appearance of the salt band in the visible region is accompanied by disappearance of the spiropyran band at about 245 mμ, described above, and the appearance of a new band at about 230 mμ. No salt is formed if the acid is added at low temperatures, probably because in the sequence:

$$\text{Spiropyran} \underset{}{\overset{a}{\rightleftharpoons}} \text{" Merocyanine "} \overset{b}{\rightleftharpoons} \text{Salt}$$

step (a) and its reverse do not take place any more under these conditions. However, if the solution is first cooled to about −100° and irradiated with ultraviolet light (broken curves) and then acid is added, the same salt is formed, indicating that step (b) is not appreciably slowed down by cooling. If an excess of acid is added at room temperature, the solution then cooled down to about −100°, and an excess of triethylamine added, step (b) above is reversed and the free merocyanine base formed, just as by irradiation of the original solution of the spiropyran. If it is assumed that the excess of acid added at room temperature shifts the equilibrium completely towards the salt, this would mean complete conversion of the spiropyran into the salt of the corresponding merocyanine. On the other hand, if an excess of acid is added at low temperature, after ultraviolet irradiation, then only that part of the spiropyran opened by irradiation will be converted into the salt. Comparison of the concentration of the salt obtained in these two ways affords another method of assessing the degree of radiative conversion of the spiropyran into the merocyanine. Compound (I) in Fig. 3a may again serve as an example. The height of the salt peak at 480 mμ, after addition of excess of acid at 25° and cooling to −100°, is 0·41 optical density unit, whereas if the acid is added at −100°, after ultraviolet irradiation, the height is only 0·36 optical density unit. The amount of conversion into the merocyanine is thus (100 × 0·36/0·41 =) 87%, in good agreement with the " probable " value of 88% given in Table 2.

The effect of addition of acid also serves to stress again the similarity between the merocyanine dyes (X) and (XI) and the coloured modification of the spiropyrans, such an addition resulting in the transformation of these dyes into salts such as (Xc). As shown by the dash-dot curves in Fig. 3, the spectra of the three salts are closely similar.

Experimental.—Irradiations and spectrophotometric determinations. These were carried out in special Dewar-type cells, in a Cary model 14 recording spectrophotometer.[8] The irradiation source was a 125 w Mazda type MB/U mercury lamp (with its envelope removed) housed in an elliptic reflector.[9] Combinations of Corning filters were used to isolate the 365 mμ line and the 365 + 313 + 303 mμ group, while an interference filter was used to isolate the 303 + 313 mμ group. The concentrations of the solutions given in the Figures refer to room temperature and are not corrected for contraction on cooling.

Solvents. The standard non-polar solvent was 2 : 1 methylcyclohexane–isopentane, freed from aromatic impurities by passage through a column of highly activated alumina. The mixture was distilled in a high vacuum from a potassium–sodium alloy directly into the cell, which was then sealed. Decalin was passed through an alumina column, as above. The

standard polar solvent was 4 : 1 absolute ethanol–methanol, both freshly distilled from potassium hydroxide.

Compounds. These were prepared as described previously.[1,4,12]

The authors are indebted to Dr. Anna Weizmann for a sample of compound (X), to Dr. E. B. Knott for a sample of compound (XI), to Mr. M. Kaganowitch for synthesizing all the other compounds investigated, and to Mrs. Nelly Castel for technical assistance.

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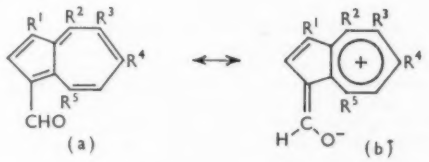
30. *Conjugated Cyclic Hydrocarbons and Their Heterocyclic Analogues. Part IV.*[1] *Dimethinecyanine Salts from 1-Formylazulenes and Heterocyclic Quaternary Ammonium Salts.*

By E. C. KIRBY and D. H. REID.

1-Formylazulenes (I—IV) condense with reactive heterocyclic quaternary ammonium salts in the presence of bases to give dimethinecyanine salts (V). The relation of this novel class of dye to known classes of cyanine salt is noted. Light absorption data for the salts are recorded.

PREVIOUS studies have shown that 1-formylazulenes (I—IV) show differences in behaviour from benzenoid aromatic aldehydes. The reduced electrophilic character of the carbonyl group is correlated with greater polarisability in the azulenes which are best represented in the ground state as resonance hybrids to which the dipolar forms (Ib—IVb) make important contributions.



(I) : $R^1 = R^2 = R^3 = R^4 = R^5 = H$
(II) : $R^1 = Me$, $R^2 = R^3 = R^4 = R^5 = H$
(III) : $R^1 = R^5 = Me$, $R^2 = R^4 = H$, $R^3 = Pr^i$
(IV) : $R^1 = R^3 = H$, $R^2 = R^4 = R^5 = Me$

This formulation accounts satisfactorily for (i) the failure of 1-formylazulenes to undergo the Cannizzaro reaction, the benzoin condensation, and oxidation to the corresponding carboxylic acids,[2] and (ii) the formation of stable hydroxymethyleneazulenium salts on treatment of 1-formylazulenes with strong acids.[3]

Alkylation increases the importance of the dipolar structures (Ib—IVb) to the resonance hybrid by inductive and hyperconjugative stabilisation, and increases thereby also the abnormality in behaviour of the aldehyde. Thus 3-formylguaiazulene (1-formyl-5-isopropyl-3,8-dimethylazulene) (III), unlike 1-formylazulene [2] (I), fails to react with

[1] Part III, *J.*, 1960, 663.
[2] Hafner and Bernhard, *Annalen*, 1959, **625**, 108.
[3] Kirby and Reid, *J.*, 1960, 494.

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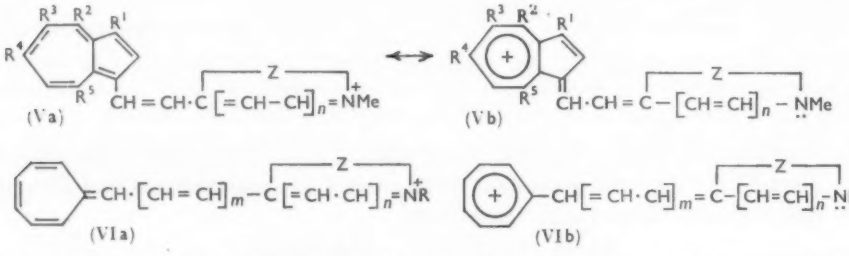
Grignard reagents,[4] behaves abnormally with lithium aluminium hydride,[4] and fails to condense with azulenes in the presence of 70% perchloric acid.[3] The position of alkylation influences the reactivity of the carbonyl group significantly for 1-formyl-4,6,8-trimethylazulene (IV) behaves like 1-formylazulene in these reactions.[2]

It has recently been shown [2] that 1-formyl-4,6,8-trimethylazulene condenses in the presence of bases with cyclopentadiene, nitromethane, diethyl malonate, and acetophenone. We now report that 1-formylazulenes condense in the presence of organic bases with



heterocyclic quaternary ammonium salts containing a reactive methyl group to form members of a novel class of dimethinecyanine salts (V) ($n = 0$ or 1; Z is the residue of

TABLE 1. *Visible absorption maxima of dimethinecyanine salts* (V) *in methanol.*

No.	Cation	X	λ (mμ) max.	log ε
1	3-[2-(Azulen-1-yl)vinyl]-2-methylisoquinolinium	ClO_4	446 *	4·53
2	2-[2-(Azulen-1-yl)vinyl]-1-methylpyridinium	ClO_4	469 *	4·64
3	2-[2-(Azulen-1-yl)vinyl]-1-methylpyridinium	I	469 *	4·63
4	2-[2-(Azulen-1-yl)vinyl]-3,4-dimethylthiazolium	I	481 *	4·58
5	2-[2-(Azulen-1-yl)vinyl]-3-methylthiazolium	ClO_4	481	4·64
6	4-[2-(Azulen-1-yl)vinyl]-1-methylpyridinium	I	482	4·69
7	2-[2-(Azulen-1-yl)vinyl]-3-methylbenzoxazolium	ClO_4	491	4·79
8	1-[2-(Azulen-1-yl)vinyl]-2-methylisoquinolinium	ClO_4	493 *	4·28
9	2-[2-(Azulen-1-yl)vinyl]-3-methylbenzothiazolium	ClO_4	514	4·78
10	2-[2-(Azulen-1-yl)vinyl]-1-methylquinolinium	ClO_4	522	4·79
11	4-[2-(Azulen-1-yl)vinyl]-1-methylquinolinium	I	541 *	4·70
12	2-Methyl-3-[2-(3-methylazulen-1-yl)vinyl]isoquinolinium	ClO_4	462	4·54
13	1-Methyl-2-[2-(3-methylazulen-1-yl)vinyl]pyridinium	ClO_4	489 *	4·65
14	3,4-Dimethyl-2-[2-(3-methylazulen-1-yl)vinyl]thiazolium	ClO_4	500 *	4·59
15	3-Methyl-2-[2-(3-methylazulen-1-yl)vinyl]thiazolium	ClO_4	502 *	4·61
16	1-Methyl-4-[2-(3-methylazulen-1-yl)vinyl]pyridinium	ClO_4	502 *	4·71
17	3-Methyl-2-[2-(3-methylazulen-1-yl)vinyl]benzoxazolium	ClO_4	509	4·79
18	3-Methyl-2-[2-(3-methylazulen-1-yl)vinyl]benzothiazolium	ClO_4	533	4·80
19	1-Methyl-2-[2-(3-methylazulen-1-yl)vinyl]quinolinium	ClO_4	543	4·80
20	1-Methyl-4-[2-(3-methylazulen-1-yl)vinyl]quinolinium	I	563	4·71
21	2-[2-(5-Isopropyl-3,8-dimethylazulen-1-yl)vinyl]-1-methylpyridinium	ClO_4	509 *	4·65
22	4-[2-(5-Isopropyl-3,8-dimethylazulen-1-yl)vinyl]-1-methylpyridinium	I	524 *	4·72
23	2-[2-(5-Isopropyl-3,8-dimethylazulen-1-yl)vinyl]-3-methylthiazolium	ClO_4	525 *	4·69
24	2-[2-(5-Isopropyl-3,8-dimethylazulen-1-yl)vinyl]-3-methylbenzothiazolium	ClO_4	550 *	4·78
25	4-[2-(5-Isopropyl-3,8-dimethylazulen-1-yl)vinyl]-1-methylquinolinium	I	592 *	4·72
26	1-Methyl-2-[2-(4,6,8-trimethylazulen-1-yl)vinyl]pyridinium	ClO_4	482 *	4·59
27	1-Methyl-2-[2-(4,6,8-trimethylazulen-1-yl)vinyl]pyridinium	I	482 *	4·59
28	3-Methyl-2-[2-(4,6,8-trimethylazulen-1-yl)vinyl]benzoxazolium	ClO_4	497	4·76
29	3,4-Dimethyl-2-[2-(4,6,8-trimethylazulen-1-yl)vinyl]thiazolium	ClO_4	499 *	4·61
30	3,4-Dimethyl-2-[2-(4,6,8-trimethylazulen-1-yl)vinyl]thiazolium	I	499 *	4·59
31	3-Methyl-2-[2-(4,6,8-trimethylazulen-1-yl)vinyl]thiazolium	ClO_4	499	4·61
32	1-Methyl-4-[2-(4,6,8-trimethylazulen-1-yl)vinyl]pyridinium	ClO_4	499	4·64
33	1-Methyl-4-[2-(4,6,8-trimethylazulen-1-yl)vinyl]pyridinium	I	499	4·64
34	3-Methyl-2-[2-(4,6,8-trimethylazulen-1-yl)vinyl]benzothiazolium	ClO_4	530 *	4·74
35	1-Methyl-2-[2-(4,6,8-trimethylazulen-1-yl)vinyl]quinolinium	ClO_4	567	4·22
36	1-Methyl-4-[2-(4,6,8-trimethylazulen-1-yl)vinyl]quinolinium	I	572 *	4·63

* Centre of very broad maximum.

[4] Reid, Stafford, and Stafford, *J.*, 1958, 1118.

a heterocyclic nucleus). The methyl group in the heterocycle is situated so that resonance occurs in the product between structures (Va) in which the positive charge is carried by quaternary nitrogen, and structures (Vb) in which the seven-membered ring has assumed the tropylium structure. The dimethinecyanine salts (V) are examples of one of several novel classes of cyanine dyes derived from the parent hypothetical structure (VI) [n and Z are as in (V), $m = 0, 1, 2$, etc.]. Structurally they occupy a position between those cyanine dyes whose cationic resonance involves tertiary and quaternary nitrogen, and the all-carbon 1,1′-azulylmethyleneazulenium salts.[3]

Heterocycles whose quaternary salts reacted with 1-formylazulene to form salts (V $R^1 = R^2 = R^3 = R^4 = R^5 = H$) were 2- and 4-methyl-pyridine and -quinoline, 2-methylbenzoxazole and -benzothiazole, 2-methyl- and 2,4-dimethyl-thiazole, and 1- and 3-methylisoquinoline. Exceptionally, 2,3-dimethylisoquinolinium perchlorate reacted sluggishly,

TABLE 2. *Condensation of* 1-*formylazulenes* (I—IV) *with heterocyclic quaternary ammonium salts.*

Procedure	Heterocyclic quaternary ammonium salt	Product no.	Yield (%)	Colour †	M. p.‡
	(a) 1-*Formylazulene* (I)				
E [a]	2,3-Dimethylisoquinolinium perchlorate	1	44	Brown [b]	>340° * [c]
A	1,2-Dimethylpyridinium perchlorate	2	78	Reddish-brown	301—302·5 *
A	,, ,, iodide	3	32	Reddish-brown	271—273 *
A	2,3,4-Trimethylthiazolium iodide	4	55	Reddish-brown	266—267 *
A	2,3-Dimethylthiazolium perchlorate	5	62	Grey-blue [d]	257 *
A	1,4-Dimethylpyridinium iodide	6	56	Brown	>291 [e]
A	2,3-Dimethylbenzoxazolium perchlorate	7	36	Brown	>320 [e]
A	1,2-Dimethylisoquinolinium perchlorate	8	46	Brown	294—297 *
A	2,3-Dimethylbenzothiazolium perchlorate	9	66	Black	307—310 *
A	1,2-Dimethylquinolinium perchlorate	10	68	Reddish-purple	298·5—300 *
A	1,4-Dimethylquinolinium iodide	11	50	Green	269—271 *
	(b) 1-*Formyl*-3-*methylazulene* (II)				
E [a]	2,3-Dimethylisoquinolinium perchlorate	12	35	Brown	>324 *
B	1,2-Dimethylpyridinium perchlorate	13	44	Black	299—301 *
B	2,3,4-Trimethylthiazolium perchlorate	14	66	Black [g]	291—292·5 *
B	2,3-Dimethylthiazolium perchlorate	15	66	Bluish-black	264—265 *
B	1,4-Dimethylpyridinium perchlorate	16	54	Green	278 *
B	2,3-Dimethylbenzoxazolium perchlorate	17	80	Green [g,h]	302—305*
B	2,3-Dimethylbenzothiazolium perchlorate	18	66	Violet-black	* [j]
B	1,2-Dimethylquinolinium perchlorate	19	96	Green	322—323 *
B	1,4-Dimethylquinolinium iodide	20	70	Black [k]	284—289 *
	(c) 1-*Formyl*-5-*isopropyl*-3,8-*dimethylazulene* (III)				
E	1,2-Dimethylpyridinium perchlorate	21	60	Black [l,m]	>205 *
E	1,4-Dimethylpyridinium iodide	22	77	Black [d,g,o]	219—227 [p]
E	2,3-Dimethylthiazolium perchlorate	23	73	Green [m]	254—256 *
E	2,3-Dimethylbenzothiazolium perchlorate	24	48	Violet-black	>150 [n]
E	1,4-Dimethylquinolinium iodide	25	36	Black [q]	250—255 *
	(d) 1-*Formyl*-4,6,8-*trimethylazulene* (IV)				
E	1,2-Dimethylpyridinium perchlorate	26	43	Dark brown	264·5—271·5 * [p]
E	,, ,, iodide	27	42	Dark brown	257·5—259·5 * [p]
A	2,3-Dimethylbenzoxazolium perchlorate	28	3	Reddish-brown [g,r]	285—290 *
D	2,3,4-Trimethylthiazolium perchlorate	29	74	Dark green	296·5—301·5 * [p]
D	,, ,, iodide	30	74	Dark green	268—270 * [p]
C	2,3-Dimethylthiazolium perchlorate	31	56	Purple	270—274 * [p]
E	1,4-Dimethylpyridinium perchlorate	32	79	Dark green	271—274 * [p]
E	,, ,, iodide	33	75	Dark green	[p]
C [t]	2,3-Dimethylbenzothiazolium perchlorate	34	59	Deep purple	276—277 [p]
C	1,2-Dimethylquinolinium perchlorate	35	63	Deep purple [u]	[p]
C	1,4-Dimethylquinolinium iodide	36	43	Dark brown	[p]

XUM

TABLE 2. (*Continued.*)

Product no.	Found (%) C	H	Hal	N	S	Formula	Required (%) C	H	Hal	N	S
1				3·7		$C_{22}H_{16}ClNO_4$				3·5	
2				4·5		$C_{19}H_{16}ClNO_4$				4·1	
3	58·0	4·6	33·7	3·8		$C_{18}H_{16}IN$	57·9	4·3	34·0	3·8	
4	52·6	4·2			8·0	$C_{17}H_{16}INS$	51·9	4·1			8·1
5			9·9	3·9	8·9	$C_{16}H_{14}ClNO_4S$			10·1	4·0	9·1
6	57·5	4·0	35·0	4·0		$C_{18}H_{16}IN$	57·9	4·3	34·0	3·8	
7	61·8	3·9	8·8	3·7		$C_{20}H_{16}ClNO_5$	62·4	4·2	9·2	3·6	
8				3·6		$C_{22}H_{16}ClNO_4$				3·5	
9	59·7	4·0	9·0	3·8	8·2	$C_{20}H_{16}ClNO_4S$	59·8	4·0	8·8	3·5	8·0
10	67·3	5·0		3·8		$C_{22}H_{16}ClNO_4$	66·8	4·6		3·5	
11	63·0	4·7		3·1		$C_{22}H_{18}IN$	62·4	4·3		3·3	
12	66·8	5·0		3·3		$C_{23}H_{20}ClNO_4$	67·4	4·9		3·4	
13	63·9	4·8	10·0	3·9		$C_{19}H_{18}ClNO_4$	63·4	5·0	9·9	4·0	
14			8·8	3·8		$C_{18}H_{18}ClNO_4S$			8·8	3·7	
15[z]			8·9		7·9	$C_{17}H_{16}ClNO_4S$			9·7		8·8
16	63·3	5·0	9·5	3·9		$C_{19}H_{18}ClNO_4$	63·4	5·0	9·9	3·9	
17	63·5	4·5	9·1	3·6		$C_{21}H_{18}ClNO_5$	63·1	4·5	8·9	3·5	
18			8·9	3·5	8·0	$C_{21}H_{18}ClNO_4S$			8·5	3·4	7·7
19	67·5	5·1		2·9		$C_{23}H_{20}ClNO_4$	67·4	4·9		3·4	
20	63·0	4·9		3·3		$C_{23}H_{20}IN$	63·2	4·6		3·2	
21				3·1		$C_{23}H_{26}ClNO_4$				3·4	
22				3·1		$C_{23}H_{26}IN$				3·2	
23				3·1		$C_{21}H_{24}ClNO_4S$				3·3	
24				2·8		$C_{25}H_{26}ClNO_4S$				3·0	
25				3·1		$C_{27}H_{28}IN$				3·0	
26	65·0	5·7	9·7	3·8		$C_{21}H_{22}ClNO_4$	65·0	5·7	9·1	3·6	
27	60·8	5·5	31·1	3·6		$C_{21}H_{22}IN$	60·7	5·3	30·6	3·4	
28	64·9	5·3		3·3		$C_{23}H_{22}ClNO_5$	64·6	5·2		3·3	
29	59·9	5·8	8·2	3·2	7·6	$C_{20}H_{22}ClNO_4S$	58·9	5·4	8·7	3·4	7·9
30	55·5	5·1		3·1		$C_{26}H_{22}INS$	55·2	5·1		3·2	
31	57·9	5·1	9·1	3·6	8·0	$C_{19}H_{20}ClNO_4S$	57·9	5·1	9·0	3·6	8·1
32	65·2	5·7	9·1	3·8		$C_{21}H_{22}ClNO_4$	65·0	5·7	9·1	3·6	
33	60·5	5·2	30·8	3·5		$C_{21}H_{22}IN$	60·7	5·3	30·6	3·4	
34	62·6	5·2	7·7	3·2	7·2	$C_{23}H_{22}ClNO_4S$	62·2	5·0	8·0	3·2	7·2
35			8·2	3·1		$C_{25}H_{24}ClNO_4$			8·1	3·2	
36	64·6	5·4		3·2		$C_{25}H_{24}IN$	64·5	5·2		3·0	

* With decomp. † Needles unless otherwise stated. ‡ Heating stage preheated to *ca.* 10° below the m. p. unless otherwise stated.

[a] Boiled for 30 min. [b] Powder. [c] Partial melting with blackening. [d] Recryst. from acetonitrile–ethanol (1 : 2). [e] Decomp. without melting. [f] Above 315° colour change from brown through grey to black. [g] Green reflex. [h] Red reflex. [i] Softens >290°. [j] Melts on block preheated to <323°. [k] Prisms. [l] Plates. [m] Recryst. from MeOH. [n] Gradual melting to a tar. [o] Flat needles. [p] Placed on heating stage at room temperature. [q] Indefinite form. [r] Washed with hot water; recryst. from EtOH. [s] Does not melt < 340°. [t] Condensation in 50 ml. of ethanol; solution concentrated to 25 ml. before crystallisation. [u] Recryst. from acetonitrile–ethanol (1 : 4). [v] Softens >235°. [w] Softens >350°. [z] No satisfactory analysis.

a result in agreement with the known lower reactivity of the 3- than of 1-methylisoquinoline and their quaternary salts.[5]

Alkylation lowers, but does not repress completely, the carbonyl reactivity of 1-formylazulene. 1-Formyl-3-methylazulene (II) behaved like the parent (I), condensing with all the heterocyclic quaternary salts cited. However, products could not be isolated after treatment of 3-formylguaiazulene or 1-formyl-4,6,8-trimethylazulene with the weakly reactive 2,3-dimethylisoquinolinium perchlorate, or after that of 3-formylguaiazulene with 2,3-dimethylbenzoxazolium perchlorate. The violet-blue product from 3-formylguaiazulene and 1,2-dimethylquinolinium perchlorate was unstable; it could not be purified by recrystallisation.

The dimethinecyanine salts (V) crystallise well from acetonitrile, and in the solid state are stable to air and light. Their visible absorption spectra consists in all cases of a single, broad absorption band lacking fine structure. Table 1 records the position and intensity

[5] Mills and Smith, *J.*, 1922, 2724; Erlenmeyer, Baumann, and Sorkin, *Helv. Chim. Acta*, 1948, **31**, 1978; Brooker and White, *J. Amer. Chem. Soc.*, 1951, **73**, 1094.

of this band for thirty-six salts. The following observations are noteworthy. (*a*) Alkylation of the azulene nucleus produces in all cases a bathochromic displacement of $\lambda_{max.}$ (Fig. 1). (i) A 3-methyl substituent produces an almost constant shift of +20 mμ (this drops to +16 mμ when the heterocyclic component is 3-isoquinoline). (ii) The same order of shift results from the combined effects of methyl substituents in the 4-, 6-, and 8-positions. (The shifts for compounds nos. 28, 35, and 36 of Table 1 deviate markedly from the mean value, being +6, +45, and +31 mμ, respectively.) (iii) Derivatives of guaiazulene show displacements of $\lambda_{max.}$ lying between +36 (compound no. 24) and +51 mμ (compound no. 25). (*b*) In each series with the same azulene nucleus, the absorption maximum shifts to longer wavelength as the heterocyclic component is changed in the order: 3-isoquinoline; 2-pyridine; 2-(4-methylthiazole), 2-thiazole, 4-pyridine; 2-benzoxazole; 1-isoquinoline; 2-benzothiazole; 2-quinoline; 4-quinoline [as an exceptional case, in the series derived from 1-formyl-4,6,8-trimethylazulene, compound no. 28 precedes compounds nos. 29—33 by a small decrement (2 mμ) in order of increasing wavelength] (see Fig. 2).

Experimental

M. p.s were determined on a Kofler-type heating stage. Visible spectra were determined with a Unicam S.P. 600 instrument. Specimens for analysis were dried for 4—6 hr. at 90°/0·1 mm. Acetonitrile was purified by successive distillations from phosphoric anhydride and freshly dried potassium carbonate

Condensation of 1-Formylazulenes with Heterocyclic Quaternary Ammonium Salts.—Condensations were by one of the following general procedures (for details see Table 2).

Procedure A. A mixture of the 1-formylazulene (0·003 mole), the heterocyclic quaternary ammonium salt (0·003 mole), piperidine (0·25 ml.), and ethanol (25 ml.) was boiled for 5 min. In most cases the product partly crystallised from the boiling solution. It was filtered off

Fig. 1.

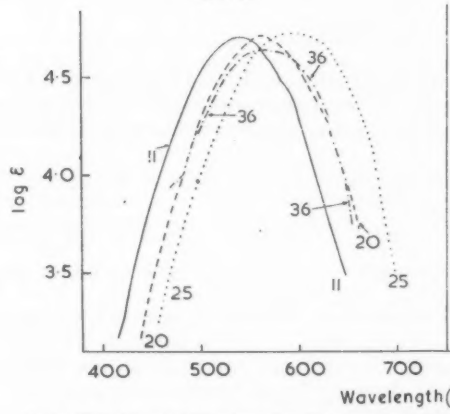
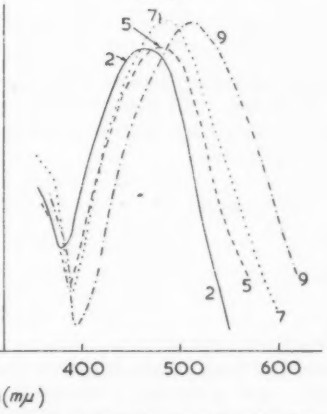


Fig. 2.



Figs. 1 and 2.—*Absorption spectra for methanol solutions of dimethinecyanine salts* (V) *(numbers refer to Table* 1).

from the cooled solution, washed with a small volume of ethanol, and, unless otherwise stated, recrystallised from acetonitrile.

Procedures B, C, D, and E. These were identical with procedure A except that the quantity of piperidine used was, respectively, 0·4, 0·5, 1 and 2 ml.

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31. *Reduction of Cholesteryl Benzoylformate (Phenylglyoxylate).*

By S. P. Bakshi and E. E. Turner.

Cholesteryl benzoylformate has been prepared. Its partial asymmetric reduction to cholesteryl mandelate and its reductive scission to phenylethylene glycol have been examined and compared with the corresponding processes with (−)-menthyl benzoylformate.

The reduction of (−)-menthyl benzoylformate (phenylglyoxylate) can take place in two stages to give (−)-menthyl mandelate or, with scission, phenylethylene glycol. We have made a number of observations, the results of which are tabulated below and compared, where possible, with those of previous workers. From them we conclude that all the reductions go in the lævorotatory sense. Sodium borohydride is the most stereoselective reducing agent used, but it was necessary to have boric acid present in order to prevent saponification of the esters by the alkali formed.

Reference	Reducing agent	Rotation of (−)-menthyl mandelate in EtOH		Rotation of HO·CHPh·CH_2·OH
McKenzie [1]	Al–Hg in Et_2O–H_2O	$[\alpha]_D^{18}$ −76·9°		
		$[\alpha]_D^{20}$ −77·6°		
McKenzie and Humphries [2]	,, ,,	$[\alpha]_D^{18\cdot5}$ −81·5°		
		$[\alpha]_D^{15}$ −80·3°		
Present work	,, ,,	$[\alpha]_D^{22\cdot6}$ −76·3°	$LiAlH_4$	
		$[\alpha]_{5461}^{22\cdot6}$ −90·8°	→	$[\alpha]_D^{25}$ −4·4° ($CHCl_3$)
Prelog *et al.*[3]	$LiAlH_4$	—		$[\alpha]_D^{20}$ −2·95° (EtOH)
Present work	,,	—		$[\alpha]_D^{21}$ −3·4° (EtOH)
				−5·2° ($CHCl_3$)
Present work	$NaBH_4$	$[\alpha]_D^{24\cdot8}$ −91·45°	$LiAlH_4$	
		$[\alpha]_{5461}^{24\cdot8}$ −110·1°	→	4 $[\alpha]_D^{22\cdot8}$ −18·4° ($CHCl_3$)

(−)-Menthyl (±)-mandelate has $[\alpha]_{5461}^{19\cdot6}$ −87·3° (EtOH).
(−)-Menthyl (−)-mandelate has $[\alpha]_{5461}^{19}$ −163·5° (EtOH) (Jamison and Turner [4]).

Cholesteryl benzoylformate has also been prepared, and has been examined with the results tabulated. All these reductions go in the dextrorotatory sense. Judged by the rotations of the phenylethylene glycols, aluminium amalgam is the most stereospecifically efficient in this case.

Reducing agent	Rotation of cholesteryl mandelate in $CHCl_3$		Rotation of HO·CHPh·CH_2·OH
Al–Hg	$[\alpha]_D^{22\cdot6}$ −16·87°	$LiAlH_4$ →	$[\alpha]_D^{21\cdot4}$ +2·66° ($CHCl_3$)
$NaBH_4$	$[\alpha]_D^{25}$ −18·69°	$LiAlH_4$ →	$[\alpha]_D^{25\cdot2}$ +1·79° (EtOH)
$Al(OPr^i)_3$	$[\alpha]_D^{21}$ −28·26°	$LiAlH_4$ →	$[\alpha]_D^{22}$ +1·09° ($CHCl_3$)
$LiAlH_4$	—		$[\alpha]_D^{21\cdot8}$ +1·14° (EtOH)

Cholesteryl benzoylformate melts first at 119—120° and solidifies to a more stable form, m. p. 128—129°, a blue-green fluorescence usually appearing between 119° and 129°. The two forms sometimes separate side-by-side from an ethanolic solution.

The sparing solubility of cholesteryl benzoylformate in ethanol prevented a study being made of the expected mutarotation based on hemiacetal formation.

Experimental

Reduction of (±)-Mandelic Acid by Lithium Aluminium Hydride.—(±)-Mandelic acid (10 g., 0·065 mole) in dry ether (200 c.c.) was added during 30 min. to lithium aluminium hydride (5 g.,

[1] McKenzie, *J.*, 1904, **85**, 1249.
[2] McKenzie and Humphries, *J.*, 1909, **95**, 1105.
[3] Prelog, Wilhelm, and Bright, *Helv. Chim. Acta*, 1954, **37**, 2217.
[4] Jamison and Turner, *J.*, 1942, 611.

0·13 mole) in dry ether (150 c.c.). Then the mixture was boiled under reflux for 2 hr., cooled, and treated with water and then with dilute sulphuric acid. The aqueous layer was extracted with ether, and the extracts were dried (K_2CO_3) and evaporated, giving phenylethylene glycol, m. p. 62—65° (7 g., 77%).

Reduction of (−)-Mandelic Acid by Lithium Aluminium Hydride.—(−)-Mandelic acid, m. p. 132—134°, $[\alpha]_D^{23\cdot6}$ −154·3° ± 0·6°, $[\alpha]_{5461}^{23\cdot6}$ −184·7° ± 0·6° (*c* 1·6430 in H_2O) (8·83 g., 0·05 mole), with lithium aluminium hydride (5 g., 0·13 mole) gave phenylethylene glycol (6·9 g., 87%). After being sublimed under reduced pressure this had m. p. 66—67°, $[\alpha]_D^{24}$ −39·9° ± 0·3°, $[\alpha]_{5461}^{24}$ −47·7° ± 0·3° (*l* 1, *c* 6·562 in EtOH), and $[\alpha]_D^{23}$ −63·8° ± 0·2°, $[\alpha]_{5461}^{23}$ −75·8° ± 0·2°, (*l* 1, *c* 9·522 in $CHCl_3$). Prelog and his co-workers [3] give $[\alpha]_D^{20}$ +40·6° (*l* 2, *c* 3·23, in EtOH) for phenylethylene glycol obtained from (+)-mandelic acid with $[\alpha]_D^{18}$ +157·5° (*l* 2, *c* 3·50, in H_2O).

Reduction of (−)-Menthyl Benzoylformate.—(a) *By lithium aluminium hydride.* A solution of (−)-menthyl benzoylformate (10 g., 0·06 mole) in dry ether (200 c.c.) was added in small portions during 30 min. to a suspension of lithium aluminium hydride (3·3 g., 0·08 mole) in dry ether (200 c.c.). Then the mixture was boiled under reflux for 30 min., cooled in ice, and worked up normally. The menthol obtained weighed 4·9 g. (90%). 4·2 g. (89%) of phenylethylene glycol were obtained, with m. p. 62—66°, $[\alpha]_D^{21}$ −3·4° ± 0·1°, $[\alpha]_{5461}^{21}$ −3·9° ± 0·1° (*c* 9·15 in EtOH), and $[\alpha]_D^{20}$ −5·2° ± 0·1°, $[\alpha]_{5461}^{20}$ −5·9° ± 0·1° (*c* 10·88 in $CHCl_3$). The optical purity was 8%. Prelog and his co-workers [3] gave m. p. 62—63°, $[\alpha]_D$ −2·95° (*l* 2, *c* 10·6 in EtOH).

(b) *By aluminium amalgam.* The (−)-ester (5 g., 0·017 mole) in moist ether (150 c.c.) was added to aluminium amalgam (~5 g.). After the reaction had subsided, the whole was shaken for 5 hr., then filtered, and the residue was washed with ether. The solution was dried (Na_2SO_4) and evaporated, giving (−)-menthyl mandelate (4·2 g., 80%), m. p. 84—86°, $[\alpha]_D^{22\cdot6}$ −76·3° ± 0·5°, $[\alpha]_{5461}^{22\cdot6}$ −90·8° ± 0·5° (*c* 1·8480 in EtOH).

To a solution of lithium aluminium hydride (1·5 g., 0·03 mole) in dry ether (75 c.c.) was added in small portions a solution of the foregoing (−)-menthyl mandelate (2 g., 0·006 mole) in dry ether (100 c.c.) at room temperature during 15 min. The products were isolated in the usual way, and yielded phenylethylene glycol (0·82 g., 89%), m. p. 64—66°, $[\alpha]_D^{23}$ −4·4° ± 0·25°, $[\alpha]_{5461}^{23}$ −5·2° ± 0·25° (*l* 1, *c* 8·340, in $CHCl_3$) (Found: C, 69·8; H, 7·3. Calc. for $C_8H_{10}O_2$: C, 69·5; H, 7·3%). The optical purity was 7%.

(c) *By sodium borohydride.* A solution of sodium borohydride (2·4 g., 0·06 mole) in water (40 c.c.) was added during 20 min. to a cooled (0°) and stirred mixture of (−)-menthyl benzoylformate (4 g., 0·013 mole), ethyl alcohol (200 c.c.), water (40 c.c.), and boric acid (8 g.). After being stirred for another 20 min. the mixture was diluted with water and acidified with dilute sulphuric acid. (−)-Menthyl mandelate was filtered off, washed with water, dissolved in chloroform, and dried (Na_2SO_4). After the removal of chloroform there was obtained (−)-menthyl mandelate (2·3 g., 57·5%), m. p. 82—84°, $[\alpha]_D^{24\cdot8}$ −91·45° ± 0·8°, $[\alpha]_{5461}^{24\cdot8}$ −110·1° ± 0·8° (*c* 1·1700 in EtOH) (Found: C, 74·6; H, 8·8. Calc. for $C_{18}H_{26}O_3$: C, 74·4; H, 9·0%).

Reduction of this crude (−)-menthyl mandelate (2 g., 0·006 mole) in dry ether (100 c.c.) with lithium aluminium hydride (1·5 g., 0·03 mole) in dry ether (75 c.c.) gave phenylethylene glycol (0·82 g., 89%), m. p. 58—62°, $[\alpha]_D^{22\cdot8}$ −18·44° ± 0·24°, $[\alpha]_{5461}^{22\cdot8}$ −21·5° ± 0·24° (*l* 1, *c* 9·1340 in $CHCl_3$) (optical purity 29%) (Found: C, 69·5; H, 7·5%).

(d) *By aluminium isopropoxide.* A mixture of (−)-menthyl benzoylformate (4 g.), aluminium isopropoxide (10 g.), and isopropyl alcohol (120 c.c.) was boiled under reflux for 1 hr. After removal of the acetone formed and the solvent, the residue was treated with ice-cold dilute sulphuric acid. Ether-extraction of the product, followed by the usual procedure, gave (−)-menthyl mandelate (2·8 g., 70%) as a colourless liquid. After 3 weeks it had changed to a wax. The smell of menthol was perceptible. It had $[\alpha]_D^{22\cdot4}$ −39·7° ± 0·4°, $[\alpha]_{5461}^{22\cdot4}$ −47·2° ± 0·4° (*c* 2·2470 in $CHCl_3$). In view of the contamination of this (−)-menthyl mandelate with menthol, no attempt was made to analyse or to reduce it with lithium aluminium hydride.

Preparation of Cholesteryl Benzoylformate.—Benzoylformyl chloride (20·8 g., 0·12 mole) in benzene (160 c.c.) was added in small portions to a solution of cholesterol (40 g., 0·1 mole) in benzene (240 c.c.) and pyridine (160 c.c.) during 30 min. at room temperature. The mixture was left overnight, then extracted twice with water, twice with dilute hydrochloric acid, twice with 5% sodium hydrogen carbonate solution, and twice with water. Evaporation of the benzene gave crude *cholesteryl benzoylformate* which, crystallised twice from acetone, formed rectangular plates (46 g., 86%), m. p. 119—120°, remelting point 128—129° (at the melting

range it showed blue-green fluorescence), $[\alpha]_D^{26\cdot6}$ −15·01° ± 0·8°, $[\alpha]_{5461}^{26\cdot6}$ −16·7° ± 0·8° (*c* 1·1790 in $CHCl_3$) (Found: C, 81·0; H, 8·55. $C_{35}H_{50}O_3$ requires C, 81·0; H, 9·7%).

Reduction of Cholesteryl Benzoylformate.—(a) *With lithium aluminium hydride.* A solution of cholesteryl benzoylformate (10 g., 0·019 mole) in dry ether (250 c.c.) was added during 30 min. to a suspension of lithium aluminium hydride (3·3 g., 0·08 mole) in dry ether (180 c.c.). The mixture was worked up in the usual way. The residue was washed with water. The cholesterol (7·2 g., 97%) had m. p. 143—145°.

Evaporation of the filtrate yielded phenylethylene glycol. After sublimation under reduced pressure it (1·35 g.) had m. p. 63—67°, $[\alpha]_D^{21\cdot8}$ +1·14° ± 0·16°, $[\alpha]_{5461}^{21\cdot8}$ +1·37° ± 0·15° (*c* 6·1240 in EtOH) (optical purity 2·7%) (Found: C, 70·0; H, 7·6%).

(b) *With aluminium amalgam.* A solution of cholesteryl benzoylformate (5 g.) in moist ether (150 c.c.) was shaken with aluminium amalgam (~5 g.) for 5 hr., then filtered and dried (Na_2SO_4). The *cholesteryl mandelate* (4 g., 78%) obtained after the removal of ether had m. p. 148—153°, $[\alpha]_D^{22\cdot6}$ −16·87° ± 0·5°, $[\alpha]_{5461}^{22\cdot6}$ −21·6° ± 0·5° (*c* 1·8820 in $CHCl_3$) (Found: C, 81·0; H, 10·15. $C_{35}H_{52}O_3$ requires C, 80·7; H, 10·1%).

To a solution of lithium aluminium hydride (1·5 g., 0·03 mole) in dry ether (75 c.c.) was added in small portions a solution of the cholesteryl mandelate (2 g., 0·003 mole) in dry ether (100 c.c.) during 25 min. The products, isolated in the usual way, afforded phenylethylene glycol (0·29 g., 54·7%), m. p. 58—64°, $[\alpha]_D^{21\cdot4}$ +2·66° ± 0·8°, $[\alpha]_{5461}^{21\cdot8}$ +3·35° ± 0·8° (*l* 1, *c* 2·472 in $CHCl_3$) (optical purity 4%) (Found: C, 69·8; H, 7·65%).

(c) *With sodium borohydride.* Sodium borohydride (1·2 g., 0·03 mole) was added in small portions to a mixture of cholesteryl benzoylformate (2 g., 0·003 mole), dioxan (250 c.c.), water (16 c.c.), and boric acid (4 g.). The pH of the mixture, after the reaction was completed, was 7. The dioxan was removed by distillation. The mixture was diluted with water, acidified with dilute sulphuric acid, and extracted with ether four times. The combined ethereal extracts were dried (Na_2SO_4). Removal of ether gave cholesteryl mandelate (1·95 g., 93%), m. p. 147—150°, $[\alpha]_D^{25\cdot4}$ −18·69° ± 0·7°, $[\alpha]_{5461}^{25\cdot4}$ −20·77° ± 0·7° (*c* 1·3240 in $CHCl_3$) (Found: C, 80·2; H, 10·1%).

Reduction of this ester (1·4 g., 0·002 mole) in dry ether (75 c.c.) with lithium aluminium hydride (1 g., 0·026 mole) in ether (50 c.c.) gave phenylethylene glycol (0·17 g., 46%), m. p. 64—66°, $[\alpha]_D^{24\cdot2}$ +1·85° ± 1°, $[\alpha]_{5461}^{24\cdot2}$ +3·08° ± 1° (*l* 1, *c* 1·7220 in $CHCl_3$), and $[\alpha]_D^{25\cdot2}$ +1·79° ± 1·8°, $[\alpha]_{5461}^{25\cdot2}$ +3·76° ± 1·8° (*l* 1, *c* 1·118 in EtOH) (optical purity 2·8%) (Found: C, 68·45; H, 7·0%).

(d) *With aluminium isopropoxide.* Cholesteryl benzoylformate (3 g.) was boiled with aluminium isopropoxide (7·5 g.) and isopropyl alcohol (180 c.c.) for 3½ hr. After removal of the acetone formed and the solvent, the residue was treated with ice-cold dilute sulphuric acid. Ether-extraction followed by the usual procedure gave cholesteryl mandelate (3 g., 92%), m. p. 125—131°, $[\alpha]_D^{21}$ −28·26° ± 0·3°, $[\alpha]_{5461}^{21}$ −33·8° ± 0·3° (*c* 2·9140 in $CHCl_3$) (Found: C, 81·2; H, 11·15%).

This (2 g.) in dry ether (100 c.c.) was reduced with lithium aluminium hydride (1·15 g.) in ether (100 c.c.), giving phenylethylene glycol (0·17 g., 32%), m. p. 62—64°, $[\alpha]_D^{22}$ +1·09° ± 1°, $[\alpha]_{5461}^{21}$ +1·27° ± 1° (*l* 1, *c* 1·738, in $CHCl_3$) (optical purity 1·5%) (Found: C, 68·8; H, 7·4%).

Dimorphism of Cholesteryl Benzoylformate.—Cholesteryl benzoylformate crystallised from ethanol in two forms that were separated by hand-picking. One formed leaflets, m. p. 119—120°. The stable form, rectangular plates melted at 128—129°. A blue-green fluorescence appeared between melting and re-solidification.

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32. *The Hydratropic Acids and the Related 2-Phenylpropanols.*

By S. P. Bakshi and E. E. Turner.

Cholesteryl (+)- and (−)-hydratropate have been obtained from the optically pure hydratropic acids, which have been reduced to the pure 2-phenylpropanols.

As a method of obtaining optically pure (+)- and (−)-2-phenylpropan-1-ol, we selected the reductive scission of cholesteryl (−)- and (+)-hydratropate, thinking that the mixture of these esters formed by the condensation of cholesterol with (±)-hydratropoyl chloride should be resolvable by crystallisation. In fact, although highly crystalline material was obtained from "cholesteryl (±)-hydratropate," the only individual compound that could be isolated was, curiously, the more soluble cholesteryl (−)-hydratropate, and this only in very small yield. In spite of extensive crystallisations from different solvents, the bulk of the material obtained contained (+)- and (−)-esters in the proportion of about 53 : 47.

Pure cholesteryl (+)- and (−)-hydratropate have been prepared from the corresponding active acids, which were obtained by resolving the (±)-acid; strychnine leads to the (+)-acid (cf. Raper [1]), and quinine to the (−)-acid (cf. Levene, Mikeska, and Passoth [2]). The (+)-acid had m. p. 31·5—32°, $[\alpha]_D^{25}$ +76·3° ± 0·6°, $[\alpha]_{5461}^{25}$ +91·7° ± 0·6° (*c* 1·613 in $CHCl_3$); the (−)-acid had m. p. 31—32°, $[\alpha]_D^{25}$ −76·1° ± 0·6°, $[\alpha]_{5461}^{25}$ −91·5° ± 0·6° (*c* 1·599 in $CHCl_3$). The best previous figures are those of Fredga [3] who recorded for the (+)-acid, m. p. 30·2—30·9°, and for the (−)-acid, m. p. 30·3—31°, $[\alpha]_D^{25}$ −75·3° (*c* 1·587 in $CHCl_3$).

Conversion of the active acids into the acid chlorides, following by condensation with cholesterol in presence of pyridine, led to cholesteryl (+)-hydratropate, $[\alpha]_D^{20}$ +10·6° ± 0·4°, $[\alpha]_{5461}^{20}$ +13·3° ± 0·4° (*c* 2·3990 in $CHCl_3$), and cholesteryl (−)-hydratropate, $[\alpha]_D^{24}$ −58·2° ± 0·6°, $[\alpha]_{5461}^{24}$ −69·9° ± 0·6° (*c* 1·6170 in $CHCl_3$).

Racemic hydratropic acid has hitherto been prepared (*a*) from benzyl cyanide by methylation and subsequent hydrolysis (Campbell and Kenyon [4]) (Mislow and Brenner [5] showed that acid so prepared contains α-methylhydratropic acid), (*b*) from hydratropaldehyde by oxidation (Arcus and Kenyon [6]), and by other, less satisfactory, methods. The simplest synthesis appeared to be by the action of carbon dioxide on 1-phenylethylmagnesium halides, but Ott [7] obtained *meso*- and racemic 2,3-diphenylbutane as the sole products from magnesium, 1-phenylethyl chloride, and carbon dioxide. We find that, when 1-phenylethyl chloride is allowed to react with magnesium with occasional shaking, the entire product is *meso*-2,3-diphenylbutane, but that with a sufficiently dilute mixture and with good stirring a solution is obtained which after reaction with carbon dioxide gives hydratropic acid and the *meso*-form of the hydrocarbon in about 58% and 22% yield respectively. This is therefore the simplest method of making hydratropic acid.

Reduction of cholesteryl (+)-hydratropate or of (+)-hydratropic acid with lithium aluminium hydride in ether gave (−)-2-phenylpropan-1-ol, $[\alpha]_{5461}^{24}$ −21·2° ± 0·02° ($l = 1$; d 1·00). Similarly, (+)-2-phenylpropan-1-ol was obtained with $[\alpha]_{5461}^{23}$ +21·02° ± 0·02°.

[1] Raper, *J.*, 1923, **123**, 2557.
[2] Levene, Mikeska, and Passoth, *J. Biol. Chem.*, 1930, **88**, 27.
[3] Fredga, *Arkiv Kemi*, 1954, **7**, 241.
[4] Campbell and Kenyon, *J.*, 1946, 25.
[5] Mislow and Brenner, *J. Amer. Chem. Soc.*, 1953, **75**, 2318.
[6] Arcus and Kenyon, *J.*, 1939, 916.
[7] Ott, *Ber.*, 1928, **61**, 2124.

Experimental

(±)-*Hydratropic Acid.*—Thoroughly dried ether (175 c.c.) and dried magnesium turnings (31 g.) were stirred together mechanically in a flask fitted with a protected reflux condenser. A mixture of 1-phenylethyl chloride (118·6 g.) and dry ether (400 c.c.) was added during 45 min. To complete the last stage of the reaction, the mixture was boiled for a further 30 min. The cooled solution was then decanted on to 350 g. of solid carbon dioxide in a 4-l. flask. The residual magnesium was twice extracted with dry ether, and the extract added to the carbon dioxide. When the latter had mostly disappeared, the mixture was acidified with concentrated hydrochloric acid, ice being added as required. The ethereal layer, together with three ethereal extracts of the aqueous layer, was extracted with 25% sodium hydroxide solution. The alkaline extract was evaporated to one-tenth of the bulk and then acidified with hydrochloric acid. The hydratropic acid was separated, dried (Na_2SO_4), and distilled. The yield was 73·5 g. (58%) and the b. p. 155°/21 mm. The ethereal layer gave *meso*-2,3-diphenylbutane (20 g.), m. p. 124—125° after two crystallisations from methanol (Paterno and Chieffi [8] gave m. p. 124—125°). Redistillation of the hydratropic acid gave 68·5 g., of b. p. 159°/25 mm., n_D^{25} 1·5204.

In our hands the synthesis of hydratropic acid from benzyl cyanide by the method of Campbell and Kenyon [4] gave a yield of about 45% but was less convenient than the above.

Optical Resolution of (±)-*Hydratropic Acid.*—Raper's method,[1] using strychnine (24 g.) in aqueous ethanol, gave strychnine (+)-hydratropate (21 g.) with $[\alpha]_D^{21}$ −30·8° ± 0·7°, $[\alpha]_{5461}^{22}$ −38·3° ± 0·7° (*c* 1·4090 in $CHCl_3$). From this, (+)-hydratropic acid was obtained with m. p. 31·5—32°, $[\alpha]_D^{25}$ +76·3° ± 0·6°, $[\alpha]_{5461}^{25}$ +91·7° ± 0·6° (*c* 1·613 in $CHCl_3$).

The combined mother-liquors from the strychnine salt were concentrated and acidified. The hydratropic acid obtained, after distillation, had $[\alpha]_{5461}^{20}$ −43·3° ± 3·0° (*c* 3·190 in $CHCl_3$). Of it, 31·6 g. were treated with 67 g. of anhydrous quinine in hot acetone solution. On cooling, quinine (−)-hydratropate separated and this, after systematic fractionation and crystallisation from acetone, gave a salt (33·4 g.), m. p. 176—177°, $[\alpha]_D^{23}$ −109·0° ± 0·6°, $[\alpha]_{5461}^{22}$ −132·0° ± 0·6° (*c* 1·7800 in $CHCl_3$). From this salt (−)-hydratropic acid was obtained, with m. p. 31—32°, $[\alpha]_D^{25}$ −76·1° ± 0·6°, $[\alpha]_{5461}^{25}$ −91·5° ± 0·6° (*c* 1·5990 in $CHCl_3$). After our work had been completed [see S. P. Bakshi (Chibber), Ph.D. Thesis, London, June, 1959], Roger and Neilson [9] recorded an incomplete resolution of (±)-hydratropic acid. Their (+)-acid failed to crystallise.

The hydratropoyl chlorides, obtained from the acid and thionyl chloride, had b. p. 81—83°/10 mm. The (+)-chloride, from the (+)-acid, had $[\alpha]_D^{22}$ +101·5° ± 0·4°, $[\alpha]_{5461}^{22}$ +124·2° ± 0·4° (*c* 2·4390 in C_6H_6), and $[\alpha]_D^{23}$ +87·8° ± 0·3°, $[\alpha]_{5461}^{23}$ +108·6° ± 0·3° (*c* 2·8460 in ether) {Booner, Zderic, and Castaetto [10] found $[\alpha]_D^{20}$ +50·5° (*c* 2·5, in ether)} (Found: Cl, 20·9. Calc. for C_9H_9ClO: Cl, 21·0%). The (−)-chloride from the (−)-acid had $[\alpha]_D^{21}$ −103·1° ± 0·4°, $[\alpha]_{5461}^{21}$ −126·5° ± 0·4° (*c* 2·3510 in C_6H_6) {Levene, Mikeska, and Passoth [2] recorded $[\alpha]_D^{24}$ −68·8° (*c* 21·496 in ether)} (Found: Cl, 21·6%).

Cholesteryl Hydratropates.—(*a*) A solution of cholesterol (55 g.), m. p. 147—148°, $[\alpha]_D^{22}$ −39·3° ± 0·4° (*c* 2·4490 in $CHCl_3$), in dry pyridine (160 c.c.) was treated with (±)-hydratropoyl chloride (28 g.) with frequent shaking. The suspension formed was kept at the room temperature for 2 hr., then heated at 100° for ½ hr. The cooled mixture was then poured into an excess of cold 5% hydrochloric acid with stirring. The precipitate was filtered off and washed first with 5% hydrochloric acid and later with cold water. It was taken up in chloroform and extracted thrice with 5% hydrochloric acid, twice with 5% sodium hydrogen carbonate solution, and thrice with water. The chloroform was removed and the residue crystallised from the minimum amount of alcohol (yield, 95%). On repeated crystallisation of this product from acetone, 86% was obtained as a mixture of cholesteryl hydratropates, which was almost unaffected by recrystallisation. One specimen had m. p. 116—117°, $[\alpha]_D^{23}$ −22·1° ± 1°, $[\alpha]_{5461}^{23}$ −25·8° ± 1° (*c* 0·9260 in $CHCl_3$) (Found: C, 83·9; H, 10·1. Calc. for $C_{36}H_{54}O_2$: C, 83·3; H, 10·5%). From the mother-liquors, by crystallisation from methanol–benzene, cholesteryl (−)-hydratropate was obtained, with m. p. 138—139°, $[\alpha]_D^{24}$ −56·5° ± 0·6°, $[\alpha]_{5461}^{24}$ −69·1° ± 0·6° (*c* 0·5390, in $CHCl_3$).

[8] Paterno and Chieffi, *Gazzetta*, 1909, **39**, II, 426.
[9] Roger and Neilson, *J.*, 1960, 627.
[10] Booner, Zderic, and Castaetto, *J. Amer. Chem. Soc.*, 1952, **74**, 5086.

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Crystallisation of the cholesteryl (±)-hydratropate from light petroleum (b. p. 60—80°), or from mixtures of methanol with benzene or chloroform, gave two products, one sparingly soluble, m. p. 116—117°, $[\alpha]_D$ −20·5° to −22·0° in $CHCl_3$ (Found, for example: C, 83·3; H, 9·5%), and another, readily soluble in most solvents, m. p. 137—138°, $[\alpha]_D$ −56° to −57° (Found, for example: C, 82·9; H, 9·9%).

(*b*) Cholesterol was condensed with (+)-hydratropoyl chloride in pyridine, and the product worked up as in (*a*). The *cholesteryl* (+)-*hydratropate* crystallised from acetone or chloroform–methanol in pearly plates, m. p. 105—106°, $[\alpha]_D^{20}$ +10·6° ± 0·4°, $[\alpha]_{5461}^{20}$ +13·3° ± 0·4° (*c* 3990 in $CHCl_3$) (Found: C, 83·9; H, 10·1%).

(*c*) Cholesterol and (−)-hydratropoyl chloride in pyridine similarly led to cholesteryl (−)-hydratropate, which crystallised from acetone in long pearly needles, m. p. 139·5°, $[\alpha]_D^{24}$ −58·2° ± 0·6°, $[\alpha]_{5461}^{24}$ −69·9° ± 0·6° (*c* 1·6170 in $CHCl_3$) (Found: C, 83·2; H, 9·8%).

Reduction of (+)- *and* (−)-*Hydratropic Acid.*—A solution of the acid in dry ether was added gradually to lithium aluminium hydride (1·5 mol.) in dry ether, with shaking. The mixture was allowed to boil under reflux for ½ hr. and then worked up normally. From pure (+)-hydratropic acid (−)-2-phenylpropan-1-ol was obtained, with b. p. 96°/10 mm., $d^{21.1}$ 1·000, $[\alpha]_D^{24}$ −17·4° ± 0·02°, $[\alpha]_{5461}^{24}$ −21·2° ± 0·2° (l = 1). Cohen, Marshall, and Woodman [11] recorded $[\alpha]_D^{20}$ −15·16°.

From pure (−)-hydratropic acid (+)-2-phenylpropan-1-ol was obtained with b. p. 100—101°/11 mm., $d^{21.6}$ 1·000 n_D^{25} 1·5238, $[\alpha]_D^{23}$ +17·23° ± 0·02°, $[\alpha]_{5461}^{23}$ +21·02° ± 0·02° (l = 1). Cohen *et al.*[11] recorded $[\alpha]_D^{20}$ +15·25°. Eliel and Freeman [12] gave b. p. 105—106°/11 mm., n_D^{25} 1·5230, $[\alpha]_D^{25}$ +3·18° ± 0·01°, for their product, which they calculated was 20·6% pure. Roger and Neilson,[9] by reducing (−)-hydratropic acid, obtained (+)-2-phenylpropan-1-ol with $[\alpha]_{5461}^{25}$ +20·54° (homogeneous).

Reductive Scission of Cholesteryl (+)-*Hydratropate.*—A solution of cholesteryl (+)-hydratropate in 15 parts of ether was added gradually to a suspension of 2 mols. of lithium aluminium hydride in 40 parts of ether, stirred under reflux. After a further ½ hr., water and then dilute sulphuric acid were added. The aqueous layer was thrice extracted with ether, and the combined ethereal extracts were washed with dilute potassium carbonate solution and then with water. After drying (Na_2SO_4), the ethereal solution was evaporated and the residue was distilled. The (−)-2-phenylpropan-1-ol (80% yield) had $[\alpha]_D^{21}$ −17·2° ± 0·02°, $[\alpha]_{5461}^{21}$ −21·1° ± 0·02° (l = 1). Cholesterol was isolated in almost theoretical yield.

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[11] Cohen, Marshall, and Woodman, *J.*, 1915, **107**, 887.
[12] Eliel and Freeman, *J. Amer. Chem. Soc.*, 1952, **74**, 923.

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33. *The Solvent-extraction of Beryllium from Aqueous Solutions of Mineral Acids by Alkyl Esters of Phosphoric Acid.*

By C. J. Hardy, B. F. Greenfield, and D. Scargill.

The solvent-extraction of beryllium from aqueous mineral acid solutions by a variety of mono- and di-alkyl esters of phosphoric acid has been studied by using the radioactive isotope ^{7}Be. The distribution coefficient (D_{Be}) has been measured as a function of the equilibration time, the nature and concentration of the aqueous acid, the purity, concentration, and structure of the ester, and the nature of the diluent in the organic phase. The time required to reach equilibrium depends upon the purity and structure of the ester and the concentration of aqueous acid, and varies from 15 min. for di-n-butyl to ~1000 min. with di-2-ethylhexyl hydrogen phosphate. The extraction of beryllium from dilute (<2M-)aqueous acid solution by the dialkyl esters is predominantly as the complex $BeA_2(HA)_2$ [A = $(RO)_2PO{\cdot}O^-$], but at higher aqueous acid concentration complexes containing the anion of the aqueous acid are probably also extracted. The structure of the alkyl group has a slight effect upon the value of D_{Be}, this value decreasing as the degree of branching increases and increasing with chain length. The value of D_{Be} varies considerably with the nature of the diluent and increases in the order chloroform < toluene < benzene < carbon tetrachloride < kerosene. Equilibrium constants for the complexes $BeA_2(HA)_2$ have been calculated for a series of alkyl groups with toluene as diluent. Formation constants for the $BeCl^+$, BeF^+, BeF_2, and BeF_3^- complexes in the aqueous phase have also been calculated from results on the variation of D_{Be} with the concentration of chloride ion and fluoride ion.

In addition to its well-established use as an alloying constituent and in the windows of *X*-ray apparatus, beryllium is used as a moderator in nuclear piles.[1] Beryllium-clad uranium dioxide fuel elements have been proposed for the Advanced Gas-cooled Reactor Experiment in the United Kingdom.[2] Since beryllium is relatively expensive it is of interest to obtain information on its chemical behaviour, particularly that relevant to the processing of the element from its ores to metal, and the recovery of the element from contaminated materials such as irradiated beryllium-clad fuel elements.

Solvent-extraction is a potentially useful method for the purification of beryllium. Many organophosphorus compounds and long-chain organic amines are now widely used for the solvent extraction of uranium and thorium from ore-leach liquors,[3] and of uranium and plutonium from solutions of irradiated fuel elements,[4] and of rare-earths.[5]

We have therefore examined the solvent extraction of beryllium from various aqueous mineral acid solutions by a variety of mono- and di-alkyl esters of phosphoric acid. The radioactive isotope ^{7}Be has been used to facilitate the measurement of the distribution coefficient of the beryllium between the aqueous and the organic phases. The mechanism of extraction of beryllium by these solvents is discussed and compared with that of other metals, and the application of the solvents for the separation of beryllium from other metals is considered.

Experimental

Preparation of Aqueous Solutions containing ^{7}Be.—^{7}Be, formed by irradiation of carbon with protons in the Harwell cyclotron, was obtained from the Isotope Division as a solution in

[1] "The Metal Beryllium," ed. White and Burke, Amer. Soc. Metals, Cleveland, 1955.
[2] U.K.A.E.A. 5th Annual Report (1958—9), H.M.S.O., London, p. 30.
[3] Brown and Coleman, "Progress in Nuclear Energy," Series III, Pergamon Press, London, 1958, Process Chemistry, Vol. II, Paper 1—2.
[4] "Progress in Nuclear Energy," Series III, Pergamon Press, London, 1958, Process Chemistry, Vol. II, Chapter 7.
[5] Peppard, Mason, and Moline, *J. Inorg. Nuclear Chem.*, 1957, **4**, 141.

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approximately M-hydrochloric acid.[6] An aliquot part (0·01 ml.) of this solution was added to the appropriate acid (10 ml.), so that 0·1 ml. of the mixture gave a γ-activity of about 10,000 counts/min. at 5% counting geometry in a standard γ-scintillation counter.

To prepare a 0·1M-beryllium solution with and without ^{7}Be tracer, a weighed excess of metallic beryllium was added to dilute sulphuric acid, and the amount dissolved was determined by weighing the residue. The solution was then diluted with the appropriate concentration of sulphuric acid to give 0·1M-beryllium and 2M-sulphuric acid. In one experiment (section f below) to investigate (*a*) the isotopic exchange in solution of ^{7}Be tracer and macroberyllium and (*b*) the dependence of D_{Be} on beryllium concentration, an aliquot part of the concentrated ^{7}Be tracer solution was added before the dissolution; and in another experiment the tracer was added to the diluted solution after the dissolution stage, and just before the determination of D_{Be}.

Solvents.—The esters used (all from Messrs. Albright and Wilson, Oldbury, Birmingham) are given in Table 1. The relative amounts of them in their mixtures were obtained by (i) potentiometric titration with 0·1N-sodium hydroxide of approximately 0·5M-solutions in toluene, and (ii) paper chromatography of the undiluted acids by a technique similar to that described previously.[7] A sample of "crude" di-n-octyl hydrogen phosphate in toluene was freed from the large amount of mono-ester by repeated washing with an equal volume of ethylene glycol, and then with water to remove traces of ethylene glycol.

TABLE 1.

Phosphoric ester	Abbrevn.	Solvent molarity monoester	diester	Phosphoric ester	Abbrevn.	Solvent molarity monoester	diester
Di-n-butyl	HDBP	<0·001	0·49	Di-n-decyl	HDNDP	0·007	0·49
Di-2-ethylhexyl	HDEHP	<0·001	0·50	Di-isodecyl ...		0·027	0·50
Di-n-octyl	HDNOP	0·10	0·39	Di "dodecyl" *	HDDP	0·006	0·47
Di-n-octyl after purifn.		<0·002	0·50	Mono-n-butyl...	H_2MBP	0·50	—
Di-iso-octyl.....		0·04	0·50	Mono "do-decyl" *.....	H_2MDDP	0·56	—

* "Dodecyl" = 1-isobutyl-3,5-dimethylhexyl.

Determination of the Distribution Coefficient for ^{7}Be.—The solvent and the aqueous phase were equilibrated in glass tubes, except for hydrofluoric acid for which Polythene tubes were used. In the experiments on the time-dependence of the extraction of beryllium the phases were stirred together for the relatively short times (up to 30 min.) and finally shaken mechanically in a stoppered tube. In all the other experiments the phases were shaken together in stoppered tubes. Equal volumes of solvent and aqueous phase (1—2 ml.) were used in distribution experiments, and the phases were separated by centrifugation. The distribution coefficient (D_{Be}) of ^{7}Be between solvent and aqueous phase was measured by γ-counting of aliquot parts of the solvent and aqueous phase after evaporation to dryness on stainless-steel trays (γ-scintillation counter); D_{Be} is defined as the number of counts from the organic phase divided by the number from an equal volume of the aqueous phase in the same time.

RESULTS

Extraction of Beryllium Esters of Phosphoric Acid.—(a) *Dependence of* D_{Be} *on equilibration time.* The dependence of D_{Be} on equilibration time was measured with the ^{7}Be initially in (i) the aqueous phase and (ii) the organic phase (by extraction of the ^{7}Be from an appropriate aqueous solution into the organic phase, and then stripping of the organic phase with fresh aqueous phase). The time required for D_{Be} to reach a constant value (Table 2) varied appreciably with the different solvents, varied slightly with aqueous acid concentration, and was independent of whether equilibrium was approached from the aqueous or the organic phase. All later experiments started with ^{7}Be in the aqueous phase.

The presence of monoester in the diester had a very considerable effect on the time required to reach equilibrium. This is illustrated by comparing (i) the "crude" di-n-octyl ester (containing ~20% of monoester) for which $t_{equil.}$ = 10—15 min., with purified material (<0·2%

[6] Mellish and Payne, A.E.R.E. Report, 1959, I/M 53.
[7] Hardy and Scargill, *J. Inorg. Nuclear Chem.*, 1959, **10**, 323.

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of monoester) for which $t_{equil.} = 300$—500 min., and (ii) the times required for the monododecyl ester ($t_{equil.}$ ~30 min.) and the didodecyl ester (containing <1% of monoester) ($t_{equil.}$ 250—500 min.). The more detailed work described below was therefore carried out only with dialkyl esters containing <0·5% of monoester.

(*b*) *Dependence of D_{Be} on the concentration of nitric acid in the aqueous phase, and on the type of phosphoric ester in the organic phase.* D_{Be} was measured for the available phosphoric esters with 0·25, 2, and 10M-nitric acid (Table 2), and also with 4 and 6M-acid for HDEHP. The values of D_{Be} vary by a factor of only about 3 in the range from di-n-butyl to di" dodecyl." A log–log plot of D_{Be} against $[HNO_3]$ for both mono- and di-esters gives a straight line with a slope of approximately −2 from 0·25 to ~3M-nitric acid, thus indicating an inverse dependence

TABLE 2. *Distribution of* ^{7}Be *in nitric acid–ester–toluene systems.*

Alkyl ester of H_3PO_4 (0·5M *)	Initial aq. HNO_3 concn. (M)	Time for equilibrn. (min.)	D_{Be}	Alkyl ester of H_3PO_4 (0·5M *)	Initial aq. HNO_3 concn. (M)	Time for equilibrn. (min.)	D_{Be}
Di-n-butyl	0·25	15	34·5	Di-iso-octyl	0·25	30	28·0
	2·0	90	0·74		2·0	~200	0·59
	10·0	~30	0·55		10·0	60	0·30
Di-2-ethylhexyl	0·25	~600	19·0	Di-n-decyl	0·25	45	54·0
	2·0	~1200	0·35		2·0	60	1·02
	10·0	350	0·15		10·0	60	0·61
Di-n-octyl	0·25	10	51·0	Di-isodecyl	0·25	90	30·2
	2·0	15	1·15		2·0	60	0·61
	10·0	10	0·74		10·0	30	0·30
Di-n-octyl	0·25	250	62·0	Di" dodecyl "	0·25	250	60·0
(purified)	2·0	400	0·98		2·0	500	1·20
	10·0	300	0·58	Mono-n-butyl	0·25—10·0	No extraction	
				Mono" dodecyl "	0·25	30	31·4
					2·0	30	0·69
					10·0	10	0·26

* For exact concentration and purity see Table 1.

of D_{Be} on $[H^+]^3$. At higher aqueous acid concentrations, D_{Be} is appreciably greater than indicated by this dependence.

(c) *Dependence of D_{Be} on phosphoric ester concentration.* Results on the variation of D_{Be} with phosphoric ester concentration are given in Fig. 1 and summarised in Table 3.

TABLE 3.

Ester Type	Ester Concn. (M)	Aqueous phase	Slope of log–log plot
HDBP	0·05—0·25	0·25M-HNO_3	2·2
HDBP	0·05—0·5	2M-HNO_3	1·5—2·0
H_2MDDP	0·14—0·56	0·25M-HNO_3	1·0
HDNOP	0·25 and 0·5	0·25, 2, 10M-HNO_3	~2
HDEHP	0·05—0·5	0·25M-HCl	1·9

(d) *Dependence of D_{Be} on acid medium.* (i) General. Values of D_{Be} for 0·5M-di" dodecyl " ester in toluene and 2M-solutions of various acids were H_2SO_4 1·75, $HClO_4$ 1·10, HNO_3 1·00, HCl 0·77, $HClO_4 + 10^{-2}$M-HF 0·65. Because 2M-hydrofluoric acid would have given a very low value of D_{Be} owing to the strong complex-binding of the beryllium cation by the fluoride ion, D_{Be} is given for 10^{-2}M-HF in 2M-$HClO_4$.

(ii) $HClO_4$, HNO_3, and HCl. The variation of D_{Be} with acid concentration for 0·5M-HDEHP–toluene and 0·25—10M-nitric, -hydrochloric, and -perchloric acid is shown in Fig. 2. Within experimental error the results for nitric and perchloric acid in the range 0·25—2M are equal, but those for hydrochloric acid are significantly lower. The lower value of D_{Be} in chloride solution is due to chloride complex-formation with the beryllium ion in the aqueous phase, and from the results the formation constant for the $BeCl^+$ complex has been calculated (see below).

(iii) H_2SO_4. Values of D_{Be} for sulphuric and nitric acid and 0·5M-didecyl ester–toluene are compared in Fig. 3. D_{Be} is higher for sulphuric acid on a molar basis, but when D_{Be} is plotted

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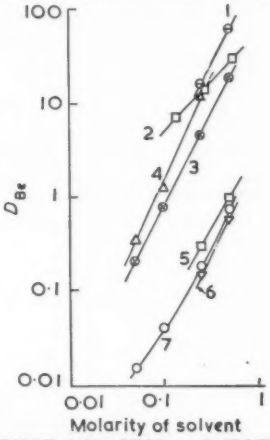
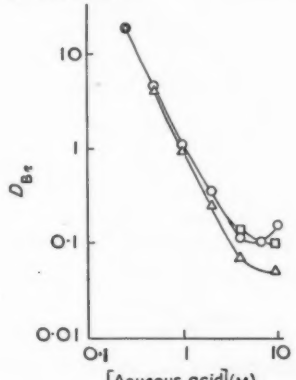
against the $[H^+]$ therein (calculated from data given by Young [8]), D_{Be} is slightly lower for sulphuric than for nitric acid at equal $[H^+]$ in the range 0·15—1·3M-H^+. The lower values are due to the relatively weak complex-binding of the beryllium ion by the hydrogen sulphate ion. The higher value of D_{Be} at ~6M-$[H^+]$ for sulphuric than for nitric acid is probably due to a combination of stronger sulphate complex-formation (to give $BeSO_4$) than nitrate complex-formation,

FIG. 1. *Variation of D_{Be} with concentration of dialkyl and monoalkyl esters.*



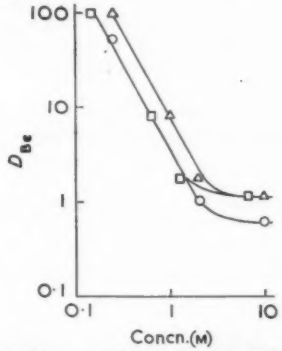
1, HDNOP–0·25M-HNO_3. 2, H_2MDDP–0·25M-HNO_3. 3, HDEHP–0·25M-HCl. 4, HDBP–0·25M-HNO_3. 5, HDNOP–2M-HNO_3. 6, HDNOP–10M-HNO_3. 7, HDBP–2M-HNO_3.

FIG. 2. *Variation of D_{Be} with concentration of aqueous acid for extraction by* 0·5M-HDEHP.



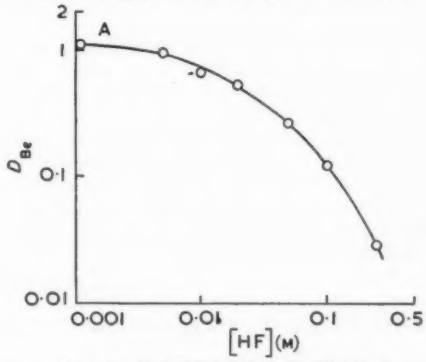
○ HNO_3. △ HCl. □ H_2SO_4.

FIG. 3. *Variation of D_{Be} with concentration of HNO_3, H_2SO_4, and H^+ in H_2SO_4, for extraction by* 0·5M-HDDP.



○ HNO_3. △ HCl. □ H^+ *in* H_2SO_4.

FIG. 4. *Variation of D_{Be} with* HF *concentration in* 2M-$HClO_4$ *for extraction by* 0·5M-HDNDP.



(A = *limit of* $[HF] = 0$ *in* 2M-$HClO_4$.)

and also to the extraction of the beryllium sulphate complex by the solvent in a similar way to the extraction of beryllium nitrate.

(iv) HF. The variation of D_{Be} with [HF] in the 2M-perchloric acid–0·5M-didecyl ester system is shown in Fig. 4. The shape of the curve can be quantitatively explained on the

[8] Young, *Rec. Chem. Progr.*, 1951, **12**, 81.

basis of fluoride complex-binding of Be^{2+} to give BeF^+, BeF_2, and BeF_3^-, and formation constants for these complexes are calculated below.

(e) *Variation of D_{Be} with the nature of the diluent.* The variation of D_{Be} with the nature of the diluent is shown in Fig. 5 for 2M-nitric acid and 0·5M-di-n-butyl ester in chloroform, carbon tetrachloride, toluene, benzene, and kerosene. The results are plotted as D_{Be} against $\log_{10} K_2$ (K_2 = dimerisation constant in the organic phase [9]) and are compared with similar results obtained previously with uranium.

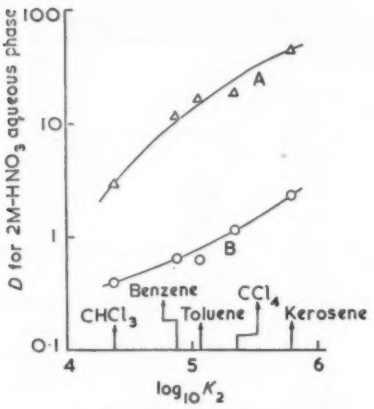


FIG. 5. *Correlation of D_{Be} and D_U with $\log_{10} K_2$ for the HDBP–2M-HNO_3 system.*
A, Uranium–0·05M-HDBP. B, Be–0·5M-HDBP

(f) *Dependence of D_{Be} on the beryllium concentration.* This is illustrated in Table 4. The conditions were—organic phase: 0·5M di-n-decylphosphoric acid/toluene; aqueous phase: 2M-H_2SO_4; varying equilibration times until equilibrium was reached.

Solution	Equilibrn. time (hr.)	D_{Be}
(i) ^{7}Be alone	1 (equil.)	1·02
(ii) 0·1M-Be + ^{7}Be (added at time of dissolution)	1	0·62
	3 (equil.)	1·00
(iii) 0·1M-Be + ^{7}Be (added immediately before equilibrn.)	1	0·54
	3 (equil.)	0·95

The conclusions from these experiments are: D_{Be} is independent of beryllium concentration in the range from tracer level to 0·1M-Be; the time to reach equilibrium depends upon the beryllium concentration (1 hr. for tracer, ~3 hr. for 0·1M); and ^{7}Be reaches isotopic equilibrium with 0·1M-Be in <60 min.

Calculation of the Equilibrium Constants for the Chloride and Fluoride Complexes of Beryllium.—(a) *Formation constant for the $BeCl^+$ complex.* The significant lowering of D_{Be} for hydrochloric compared with perchloric and nitric acid solutions (Fig. 2) is due to chloride complex-binding of the Be^{2+} ion in the hydrochloric acid solution.

The equilibrium constant, K_1, for the $BeCl^+$ complex formed by the equilibrium $Be^{2+} + Cl^- \longrightarrow BeCl^+$ is defined by:

$$K_1 = [BeCl^+]/[Be^{2+}][Cl^-]$$

The value of D_{Be} in the absence of chloride ions is given by

$$D_{Be} = [Be]_{org}/[Be]_{aq} = [BeA_2(HA)_2]_{org}/[Be^{2+}]_{aq}$$

in which A represents ester ion. In the presence of chloride ions D'_{Be} is given by:

$$D'_{Be} = [BeA_2(HA)_2]_{org}/([Be^{2+}]_{aq} + [BeCl^+]_{aq})$$

It follows that $K_1 = (x - 1)/[Cl^-]_{aq}$, where $x = D_{Be}/D'_{Be}$. Values of K_1 obtained from

[9] Hardy and Scargill, *J. Inorg. Nuclear Chem.* 1959, **11**, 128.

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the comparison of distribution coefficients in perchloric and hydrochloric acid respectively (Fig. 2) are:

	HDEHP				HDDP
$[HCl]_{aq}$ (M)	0·5	2	4	9·4	2
K_1 (mole^{-1})	0·22	0·20	0·25	0·20	0·21

The mean value of $K_1 = 0{\cdot}22 \pm 0{\cdot}03$ mole^{-1} is obtained, and is independent of ionic strength n the above range within experimental error.

(b) *Equilibrium constants for the fluoride complexes of beryllium.* The gross equilibrium constants for

$$Be^{2+} + nHF \rightleftharpoons BeF_n^{(2-n)+} + nH^+ \ (n \leqslant 3)$$

defined by $$*\beta_n = [BeF_n][H^+]^n/[Be^{2+}][HF]^n$$

can be calculated from the variation of D_{Be} with [HF] in perchloric acid (Fig. 4).

$$\text{Total } [Be]_{aq} = C_M = [Be^{2+}] + [BeF^+] + [BeF_2] + [BeF_3^-] = [Be^{2+}]x$$

where $$x = 1 + *\beta_1 \frac{[HF]}{[H^+]} + *\beta_2 \frac{[HF]^2}{[H^+]^2} + \cdots\cdots$$

Also, when no fluoride is present we have:

$$D_{Be} = [BeA_2(HA)_2]_{org}/[Be^{2+}]$$

and $$D'_{Be} = \frac{[BeA_2(HA)_2]_{org}}{([Be^{2+}] + [BeF^+] + [BeF_2] + [BeF_3^-])} = \frac{[BeA_2(HA)_2]_{org}}{[Be^{2+}]x}$$

provided that no fluoride-complex of beryllium is extracted. Hence $x = D_{Be}/D'_{Be}$ and a plot of $(x - 1)/[HF]$ against [HF] will give a straight line at low values of [HF], *i.e.*, where the BeF_3^- complex is not present in significant amount. At higher values of [HF], a curve will be obtained if the BeF_3^- complex becomes significant. In the straight-line region the slope gives $*\beta_2/[H^+]^2$ and the intercept on the $(x - 1)/[HF]$ axis gives $*\beta_1/[H^+]$. Substitution of $*\beta_1$ and $*\beta_2$ in the general equation for higher values of [HF] enables the value of $*\beta_3$ to be calculated.

An approximate straight line is obtained up to 0·1M-hydrofluoric acid, and values of $*\beta_1 = 97$ and $*\beta_2 = 1290$ are obtained. Substitution of these values in the general equation gives $*\beta_3 = 3100$. From these three constants the value of D'_{Be} has been calculated for each [HF] in Fig. 4, and these values are compared below with the experimental values. The agreement is very good.

[HF] (M)	0·005	0·01	0·02	0·05	0·10	0·25
D'_{Be} (calc.)	0·88	0·72	0·52	0·26	0·12	0·028
D'_{Be} (expl.)	0·95	0·65	0·52	0·26	0·12	0·028

For comparison of $*\beta_n$ with other published constants see below.

Discussion

The extraction of metals from aqueous solution by dialkyl hydrogen phosphates (HA) has been studied in detail recently by a number of workers [3,5,10–15] and has usually been described by the principal reaction:

$$M_{aq}^{n+} + n(HA)_{2,org} \rightleftharpoons MA_n(HA)_{n,org} + nH^+_{aq}$$

for low concentrations of the metal and an excess of the ester HA. The predominant complex in the organic phase is usually the monomer $MA_n(HA)_n$; however, the presence of the complex MA_n has been confirmed by Dyrssen and Krasovec [10] for U(VI)–HDBP–$HClO_4$

[10] Dyrssen and Krasovec, *Acta Chem. Scand.*, 1959, **13**, 561.
[11] Baes, Zingaro, and Coleman, *J. Phys. Chem.*, 1958, **62**, 129.
[12] Hardy, A.E.R.E. Report, 1959, R-3267.
[13] Dyrssen and Liem Djiet Hay, *Acta Chem. Scand.*, 1960, in the press.
[14] Dyrssen, *Acta Chem. Scand.*, 1957, **11**, 1277.
[15] Hardy and Scargill, A.E.R.E. Report, 1959, R-2945.

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at low concentrations of HDBP in the diluent hexone (isobutyl methyl ketone). With increasing metal concentration, polymers are formed, for example, $HA_2UO_2A_2UO_2\ldots A_2UO_2A_2H$ in the U(VI)–HDEHP–$HClO_4$ system.[11]

Other extraction reactions are possible from aqueous solutions in which the anion (*e.g.*, nitrate, chloride) of the mineral acid can form complexes with the metal cation. The importance of the extraction of uranyl nitrate by HDBP relative to the extraction of the uranyl ion has been discussed in detail by Hardy,[12] and equilibrium constants for the following reactions have been calculated:

$$UO_{2,aq}^{2+} + 2(HDBP)_{2,org} \longrightarrow UO_2(DBP)_2(HDBP)_{2,org} + 2H_{aq}^{+}\colon\ K = 3{\cdot}6 \times 10^4$$
$$UO_{2,aq}^{2+} + 2NO_{2,aq}^{-} + (HDBP)_{2,org} \rightleftharpoons UO_2(NO_3)_2(HDBP)_{2,org}\colon\ K = 46\ \text{moles}^{-3}$$

The extraction of beryllium from nitrate, chloride, and sulphate solution by dialkyl hydrogen phosphates follows the same pattern as the extraction of uranium from nitrate solution, *i.e.*, D_{Be} decreases with increasing $[H^+]$ at low (<3M-)aqueous acid concentration, and increases with aqueous acid concentration at $> \sim$6M. It is therefore very likely that from >3M-aqueous acid nitrate, chloride, and sulphate complexes are extracted in addition to the $BeA_2(HA)_2$ complex.

The structure of the alkyl group in ester has a slight effect on the magnitude of D_{Be} at a given concentration of ester and aqueous acid. The values of D_{Be} relative to HDEHP = 1 (Fig. 1, 0·25M-HNO_3) and the order of extraction on a mole basis are:

Di-2-ethylhexyl	1	Di-n-butyl	1·82
Di-iso-octyl	1·47	Di-n-octyl	2·68
Mono" dodecyl "	1·58	Di-n-decyl	2·84
Di-isodecyl	1·58	Di" dodecyl "	3·15

The value of D_{Be} is therefore lower the greater the degree of branching of the alkyl groups for a given carbon number, *e.g.*, 2-ethylhexyl < iso-octyl < n-octyl. Also D_{Be} increases with chain length for n-alkyl groups, *e.g.*, n-butyl < n-octyl < n-decyl.

The rate of attainment of equilibrium depends upon the purity and structure of the ester, and upon the concentration of mineral acid in the aqueous phase. The importance of purity on the rate has been illustrated for the di-n-octyl ester but the absolute value of D_{Be} is not appreciably affected. Comparison of HDBP, HDEHP, and HDNOP, all >99·8% pure, indicates that the rate of attainment of equilibrium is lower the longer the alkyl chain and the more branched the chain. These effects are probably due to steric hindrance to the attachment of a number of molecules of ester HA or ion A^- round such a small cation as beryllium (the same esters reach equilibrium much more rapidly with a large cation such as uranyl [3,12]) and also to the need to displace the strongly bound water in the primary hydration sheath.

The extraction of beryllium by mono" dodecyl " dihydrogen phosphate (H_2A) is proportional to the first power of its concentration and to $[H^+]^{-2}$ at <3M-aqueous acid. The simple equation $Be_{aq}^{2+} + H_2A_{org} \rightleftharpoons BeA_{org} + 2H_{aq}^{+}$ can therefore be used to represent equilibrium in the absence of further information on the exact nature of H_2A in the system studied, *e.g.*, dimerisation or polymerisation. The rate of extraction of beryllium by the mono" dodecyl " ester is higher than for the diester, probably owing to the greater ease of complex-formation for the small beryllium ion by one monoester molecule (2 replaceable hydrogen atoms in OH groups attached to the same phosphorus atom) than by two diester molecules, the first of which may sterically hinder the second.

The nature of the diluent has a considerable effect on the extraction of beryllium by the esters. The highest value of D_{Be} was obtained with kerosene, and if the values of D_{Be} for other diluents are expressed relative to it the following reduction factors are obtained:

Diluent	Kerosene	CCl_4	C_6H_6	$CHCl_3$
Reduction factor	1	2·0	3·5	5·8

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This effect has also been found for uranium(VI),[12] and has been studied by Dyrssen and Liem Djiet Hay [13] for europium(III) and americium(III). Extraction of the metal ion increases as the extent of interaction of the diester monomer with the diluent decreases, and the extent of interaction is indicated by the value of K_d, the distribution coefficient of the HA monomer between the two phases (and also by the value of K_2, the dimerisation constant of HA in the diluent, since K_2 increases as K_d decreases).

Equilibrium constants for beryllium–diester complexes have been calculated from the overall equations:

$$Be_{aq}^{2+} + 2(HA)_{2,org} \rightleftharpoons BeA_2(HA)_{2,org} + 2H_{aq}^{+}$$

$$\log_{10} K = \log_{10} D_{Be} + 2 \log_{10} [H^+]_{aq} - 2 \log_{10} (C_A/2)$$

in which C_A is the total molar concentration of HA in the system. Values of $\log_{10} K$ for 0·25M-nitric acid and toluene are: Bu^n 1·55, 2-ethylhexyl 1·28, iso-octyl 1·45, n-octyl 1·71, isodecyl 1·48, n-decyl 1·73, and " dodecyl " 1·78.

Comparative values for other metals calculated from data obtained under similar conditions are:

Metal	Alkyl group and diluent	$\log_{10} K$	Ref.
U(VI)	n-butyl/toluene	4·55	12
U(VI)	n-butyl/$CHCl_3$	3·58	10
Y(III)	n-butyl/$CHCl_3$	3·20	14
La(III)	2-ethylhexyl/hexane	−2·52	5

The extraction of Be^{2+} relative to other cations is illustrated for the HDBP–diluent–dilute nitric acid system, Hardy's value [15] for zirconium(IV) and Dyrssen's [13] for the other metals being used: Zr(IV) > Sc(III) > U(VI) > Y(III) > Be(II) > Eu(III) > Am(III) > La(III) > Ca(II) > Sr(II). It will therefore be possible to extract and separate selectively Zr(IV), Sc(III), and U(VI), from solutions containing Be(II) in dilute nitric acid, and to extract Be(II) from solutions containing La(III), Ca(II), and Sr(II).

The extraction of beryllium by dialkyl hydrogen phosphates can be contrasted with the extraction by tri-n-butyl phosphate (TBP) from nitric and perchloric acid solution.[16] With perchloric acid D_{Be} has the same general trend with $[HClO_4]$ as uranium(VI),[17] and it seems likely that the beryllium exists in the organic phase in the form of hydrated ions which are solvated by TBP, *e.g.*, $Be^{2+}(H_2O)_x(TBP)_2$, rather than as neutral molecules such as $Be(NO_3)_2(TBP)_2$ or $Be(ClO_4)_2(TBP)_2$. The rate of extraction by TBP is much higher than by dialkyl hydrogen phosphates (which generally have to displace the strongly bound water of hydration to form a chelate complex) as would be expected if the TBP molecules are co-ordinated through phosphoryl-oxygen groups to the water molecules around the Be^{2+} ion.

Beryllium can be placed in the following order of extraction from 2M-nitric acid by 100% TBP relative to the many other elements which have been studied: [18,19] U(VI) > Pu(VI) > Th(IV) > Am(III) > Ce(III), Zr(IV), Y(III) > Be(II) > Zn(II) > Co(II).

It is comparatively easy to separate uranium(VI) and plutonium(IV) from beryllium(II) by extraction with tributyl phosphate from the solution which would be obtained by dissolution of an irradiated beryllium-clad nuclear fuel element in nitric acid. The beryllium(II) would be discarded with the fission products in the highly active aqueous waste solution from the solvent-extraction process. It would, however, be very difficult to recover the beryllium(II) selectively from this waste solution by extraction with tributyl phosphate or with dialkyl hydrogen phosphates because many of the fission products [*e.g.*, zirconium(IV), yttrium(III)] have higher extraction coefficients than beryllium(II).

Equilibrium constants have been calculated (see Results) for the $BeCl^+$ complex, and

[16] Hardy, Greenfield, and Scargill, A.E.R.E. Report, 1960, R-3316.
[17] Hesford and McKay, *J. Inorg. Nuclear Chem.*, 1960, **13**, 165.
[18] McKay and Healy, " Progress in Nuclear Energy," Series III, Pergamon Press, London, 1958, Vol. II, Appendix III.
[19] Hardy, unpublished work on the TBP extraction of Zn(II) and Co(II).

for the first three fluoro-complexes of Be^{2+}. The values for the *consecutive* fluoro-equilibrium constants, $*K_n$, defined by

$$*K_n = [BeF_n][H^+]/[BeF_{n-1}][HF]$$

are compared below with other published values.[20] No other value for the chloro-complex has been published.

Complex	Method †	Ionic strength and medium	Temp.	n in $\log_{10} *K_n$ 1	2	3	4	Ref.
$BeCl^+$	A	0·5—6, HCl	20°	$-0·66(K_1$, not $*K_1)$				This work
$BeF_n^{(2-n)+}$ ...	A	2, $HClO_4$	20	1·99	1·12	0·38	—	This work
	B	0·5, $NaClO_4$	25	2·11	0·90	−0·17	—	*a*
	B	0·5, $NaClO_4$	25	2·12	0·84	0·03	—	*b*
	C	Various	?	2·89	1·94	0·56	−1·0	*c*

† A, Solvent extraction; B, e.m.f. with redox electrode; C, calorimetry, etc. Refs.: *a*, Yates and Dodgen, Amer. Chem. Soc. 122nd Meeting, Sept. 1952, Abs. 18P; *b*, Yates, Thesis, State Coll., Washington, 1955, Univ. Microfilms 15,662. *c*, Kleiner, *Zhur. obshchei Khim.*, 1951, **21**, 18.

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Chemistry Division, Atomic Energy Research Establishment,
Harwell, Berks. [*Received, July 5th*, 1960.]

[20] "Stability Constants," Part II, Inorganic Ligands, *Chem. Soc. Spec. Publ.* No. 11, London, 1958.

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34. *Tautomerism in the Solid State. Part I. Thermochromism of Heterocyclic Phenols.*

By A. G. Cairns-Smith.

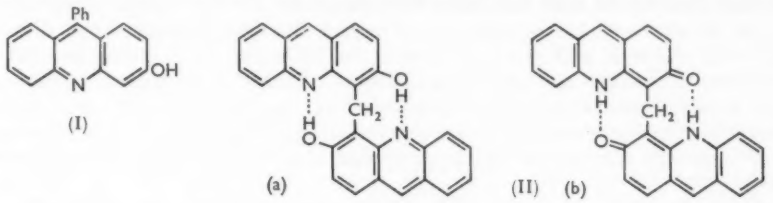
Derivatives of 2-hydroxyacridine and 2-hydroxyphenazine have been prepared which incorporate a mechanism for internal tautomeric transfer of protons. Some of these compounds are polychromic and each has at least one crystalline modification which is thermochromic. It is proposed that the thermochromism is due to a temperature-dependent disordering of protons on hydrogen bonds.

The yellow crystals of 2-hydroxy-5-phenylacridine (I) are converted into a red powder when they are crushed. This change in colour was attributed by Kehrmann and Matusinsky [2] to a tautomeric change from a lactim to a lactam structure. A later more detailed study [1] confirmed this general explanation and it was then proposed that tautomerisation was facilitated by hydrogen bonds which were postulated to exist in the crystals between all the oxygen and nitrogen atoms. This paper is concerned with the preparation and properties of model compounds which would be expected to contain internal hydrogen bonds such that tautomerisation between differently coloured structures can occur without solvent or catalyst.

Reaction of Formaldehyde with 2-Hydroxyacridine.—When an alcoholic suspension of 2-hydroxyacridine is warmed with formaldehyde and sodium acetate, a red solution is formed from which a dark red solid is rapidly precipitated. There is no evidence of polymerisation and the product can be recrystallised from dioxan without further purification. The methylene bridged structure (II) has been assigned to this product from the following evidence.

[1] Part II, Campbell and Cairns-Smith, *J.*, 1961, in the press.
[2] Kehrmann and Matusinsky, *Ber.*, 1912, **45**, 3498.

The purity of the product suggests that there is only one reactive position in the 2-hydroxyacridine molecule. Ultraviolet absorption spectra in different solvents show that this position must be a carbon atom, since lactim–lactam tautomerism, as shown by

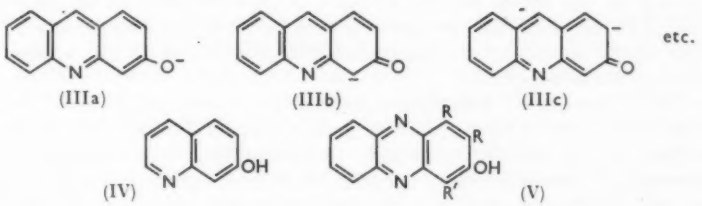


2-hydroxyacridine [3] and 2-hydroxy-5-phenylacridine,[1] is still evident. The acidic hydrogen atom has therefore not been substituted. Elemental analysis favours a methylene-bridged rather than an hydroxymethylated structure.

β-Naphthol reacts quantitatively with formaldehyde under mild conditions to give 1,1′-methylenedi-β-naphthol.[4] The greater relative reactivity of the 1-position in β-naphthol can be attributed to the possibility of localising a negative charge there without disrupting the aromaticity of the adjacent ring.[5] A similar argument applies with added force to 2-hydroxyacridine. The charge on the ion (III) may be localised at $C_{(1)}$ while leaving the aromaticity of the adjacent quinoline system intact: localisation at any other carbon atom must disrupt the aromatic nature of the whole molecule.

7-Hydroxyquinoline (IV), 2-hydroxy-5-phenylacridine (I), 2-hydroxyphenazine (V; R = R′ = H), and 2-hydroxy-3,4-dimethylphenazine (V; R′ = H, R = Me) all react with formaldehyde under the same conditions as does 2-hydroxyacridine. There is no such reaction with formaldehyde and 2-hydroxy-1,3,4-trimethylphenazine (V; R = R′ = Me).

There is evidence that in the 2-hydroxyacridine–formaldehyde product the acidic hydrogen atoms are both involved in internal hydrogen bonds: the bridged compound is more soluble in chloroform and runs much more quickly on alumina than does 2-hydroxyacridine itself; but it is less soluble in alcohol and quite insoluble in hot sodium hydroxide solution. This last point is in marked contrast to 2-hydroxyacridine, and might by itself suggest that the acidic hydrogen atoms are no longer present in the formaldehyde product.



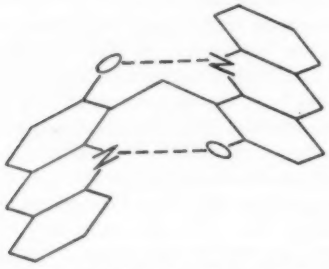
But the spectra show clearly that this is not so. The apparent contradiction can be resolved if it is assumed that the methylene bridge is formed between the carbon atoms in the 1-positions, and that both acidic hydrogen atoms are involved in hydrogen bonds which allow movement of the protons between the oxygen and nitrogen atoms while preventing their ready removal from the molecule as a whole.

The Figure illustrates the internally hydrogen-bonded arrangement envisaged. With the long axes of the acridine nuclei parallel the length of each hydrogen bond will be

[3] Albert and Short, *J.*, 1945, 760.
[4] Fries and Hubner, *Ber.*, 1906, **39**, 439.
[5] Dewar, " The Electronic Theory of Organic Chemistry," Clarendon Press, Oxford, 1949, p. 175.

2·5 Å; this is rather short for bonds of this type, but with such an arrangement each hydrogen bond will be as nearly linear as is possible. Other conformations with equivalent hydrogen bonds may be obtained by rotating each of the carbon–carbon bonds of the methlyene bridge by the same amount in the same sense; thus the length of each hydrogen bond can be increased to the more usual oxygen–nitrogen hydrogen-bond distance of about 2·8 Å,[6] although with this arrangement the hydrogen atoms are further out of the line between the oxygen and the nitrogen atoms. Probably the favoured conformation will give a pair of equivalent hydrogen bonds of between 2·5 and 2·8 Å. In any case the approximation to ideal conditions for the formation of hydrogen bonds, reviewed by Hunter,[7] is closer in this system than in most small molecules containing internal hydrogen bonds.

Dimedone–formaldehyde in the enolic form can have a similar pair of hydrogen bonds (VI); this probably accounts for the great difference in solubility in hydrogen-bonding solvents between dimedone and dimedone–formaldehyde.



Internally hydrogen-bonded conformation of 1,1′-methylenedi-2-hydroxyacridine.

According to Chmielewska and Ciercierska [8] 3-substituted derivatives of 4-hydroxycoumarin (VII) at concentrations of about 10^{-5} mole/l. in 96% aqueous alcohol exist exclusively as anions, whereas 3,3′-methylenedi-4-hydroxycoumarin is un-ionised. Here again a pair of internal hydrogen bonds seems probable (VIII).

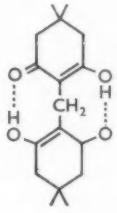
Since the ultraviolet spectra of 1,1′-methylenedi-2-hydroxyacridine show all the absorption bands typical of lactim and lactam structures, and since the relative contributions change with change of solvent, the solutions must contain mixtures rather than a resonance hybrid of the structures (IIa) and (IIb): there must be two positions for the hydrogen atoms on the bonds and the energies of these bonds must be mainly electrostatic. This is in line with the conclusion drawn by Burawoy, Salem, and Thompson [9] from a study of the ultraviolet spectra of derivatives of the internally hydrogen-bonded compound 1-phenylazo-2-naphthol.

Colour Effects shown by 1,1′-Methylenedi-2-hydroxyacridine in the Solid State.—As a model for the behaviour of 2-hydroxy-5-phenylacridine in the solid, 1,1′-methylenedi-2-hydroxyacridine is not entirely successful. It crystallises from chlorobenzene in red prisms and from chloroform in orange needles: these have the same crystal structure and give similar red powders on profound grinding, but heating does not greatly affect the colours of the crystals or of the powders. It was not possible to prepare very satisfactory films of the ground forms for ultraviolet spectroscopy in this case, but the results suggested that both the lactim and the lactam form are present. Infrared spectra were complex and difficult to interpret, but the absence of bands in the normal OH and NH regions suggests strong hydrogen-bonding. From *X*-ray powder photographs it seems that lattice disintegration, if it occurs on grinding, is not so extensive as in 2-hydroxy-5-phenylacridine.[1]

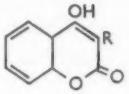
[6] Robertson, "Organic Crystals and Molecules," Cornell Univ. Press, New York, 1953, p. 243.
[7] Hunter, *Progr. Stereochem.*, 1954, **1**, 224.
[8] Chmielewska and Ciercierska, *Przemysl. Chem.*, 1952, **31** (8), 253 (*Chem. Abs.*, 1953, **47**, 9773d).
[9] Burawoy, Salem, and Thompson, *J.*, 1952, 4793.

XUM

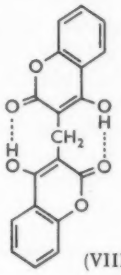
The absorption spectra of 1,1′-methylenedi-2-hydroxyacridine are similar to those of other 2-hydroxyacridine derivatives: the pure lactim form should be yellow and the pure lactam form red. In fact crystals of various intermediate shades are obtained. This suggests that in these crystals both forms of the molecule may be present: that, as in



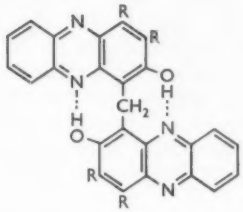
(VI)



(VII)



(VIII)



(IX)

2-phenylazo-1-naphthol [10] and some hydroxy-anils,[11] the protons may become disordered on hydrogen bonds between the oxygen and nitrogen atoms. This view is strengthened by the observation that crystals of 1,1′-methylenedi-2-hydroxyacridine become much paler on cooling: the red crystals become orange and the orange ones yellow at the temperature of liquid nitrogen. Disordered hydrogen bonds which become more ordered on cooling are known in ice [12] and in potassium dihydrogen phosphate.[13]

The thermochromism of 1,1′-methylenedi-2-hydroxyacridine is continuous and immediately reversible. That it occurs without major change in crystal structure can be seen by examining the crystals under the microscope during cooling.

There are variations in the strength of the thermochromism shown by different samples which, like the variations in the initial colours, seem to depend on the state of perfection of the crystal lattice; generally, well-crystallised samples are paler and show thermochromism more strongly than rapidly crystallised samples or ones which have been heavily ground. Such poor samples may be improved by heating them at 100° for a few hours.

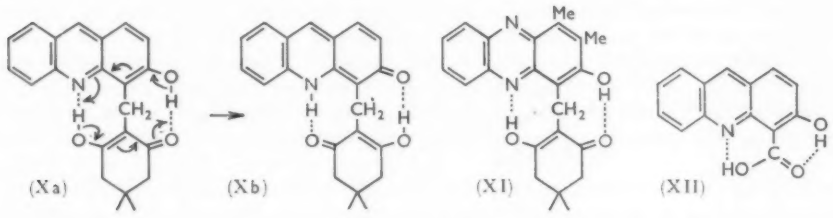
Other Related Compounds showing Thermochromism in the Solid State.—1,1′-Methylenedi-(2-hydroxy-5-phenylacridine) crystallises in orange needles from benzene and in red prisms from dioxan. The behaviour of this compound is closely similar to that of 1,1′-methylenedi-2-hydroxyacridine.

2-Hydroxyphenazine derivatives generally show tautomerism in solution. None of these has been reported as showing thermochromism in the solid state although several examples of polychromism among them have been found by John.[14] In these cases the polychromism is between the extreme lactim and lactam colours of yellow and violet. (The ultraviolet spectrum of the violet form of 2-hydroxy-1,3,4-trimethylphenazine shows that here the molecule is entirely in the lactam state.) From the spectra in solution, the relative stability of the lactam form appears to be smaller with 2-hydroxyphenazine derivatives [15] than with the corresponding acridines,[3] but the introduction of methyl groups seems to increase it.

1,1′-Methylenedi-2-hydroxyphenazine (IX; R = H) and its tetramethyl derivative (IX; R = Me) were prepared and both were found to be thermochromic in the solid state. 1,1′-Methylenedi-2-hydroxyphenazine shows only slight thermochromism, the yellow form obtained from chlorobenzene becoming reversibly dull orange between 200° and

[10] Hadzi, *J.*, 1956, 2143.
[11] Cohen, Hirshberg, and Schmidt in "Hydrogen Bonding," ed. Hadzi, Pergamon Press, London, 1959, p. 293.
[12] Pauling, *J. Amer. Chem. Soc.*, 1935, **57**, 2680.
[13] Bacon and Pease, *Proc. Roy. Soc.*, 1955, *A*, **230**, 359.
[14] John, *Angew. Chem.*, 1947, **59**, 188.
[15] Badger, Pearce, and Pettit, *J.*, 1951, 3204.

300°. 1,1′-Methylenedi-(2-hydroxy-3,4-dimethylphenazine) is both polychromic and thermochromic. Rapid crystallisation from toluene gives yellow needles which show no thermochromism; however, when these are left in contact with toluene for several hours, or



crystallise slowly, compact brick-orange crystals are obtained which are thermochromic both above and below room temperature. At −180° these crystals are yellow. Heating changes the colour, through dull orange and brick-red, to chocolate-brown at about 280°. These colour changes are immediately reversible. That they should be towards brown rather than red is to be expected on the proton-transfer theory: as the temperature rises, more and more of the deep violet lactam structures contribute to the colour of the crystals.

It seems that to produce a compound showing thermochromism in the solid from a 2-hydroxyacridine or 2-hydroxyphenazine derivative it is necessary to provide a mechanism whereby the proton may be transferred from the oxygen to the nitrogen atom by an internal rearrangement. This requirement should be fulfilled in compounds such as (X) and (XI).

The reaction which normally leads to the formation of 1,1′-methylenedi-2-hydroxyacridine gives, when carried out in the presence of a large excess of dimedone, not only a large amount of dimedone–formaldehyde and a small amount of the normal product, but also a good yield of the unsymmetrical compound (X). In its ultraviolet and visible absorption spectra in different solvents this compound (X) again shows the lactim–lactam tautomerism typical of the 2-hydroxyacridine nucleus.

The compound (X) is quite strongly thermochromic, the bright red crystals becoming reversibly pale orange at the temperature of liquid nitrogen.

The compound (XI) was prepared similarly from 2-hydroxy-3,4-dimethylphenazine. The crude product was slightly thermochromic at low temperatures. Recrystallisation from toluene gave dull yellow crystals which were still only slightly thermochromic, but a very pure sample of these changed during a few weeks into dark reddish-brown crystals which were strongly thermochromic, becoming bright yellow at the temperature of liquid nitrogen.

Unsuccessful attempts were made to prepare the simplest possible derivative of 2-hydroxyacridine incorporating a potential proton-transfer mechanism, namely, 2-hydroxyacridine-1-carboxylic acid (XII).

2-Hydroxyacridine and 2-hydroxyphenazine derivatives generally show a very slight thermochromism in solution. There is probably no particular significance in this since one would expect an equilibrium between tautomers to be influenced by temperature: in all the cases studied these colour changes were in the opposite direction to those shown by the bridged compounds in the solid.

The existence of 1,1′-methylenedi-(2-hydroxy-3,4-dimethylphenazine) in both a thermochromic and a non-thermochromic modification emphasises that the crystal structure as well as the molecular structure is important in determining the thermochromism. Even the state of perfection of the lattice seems to be significant. The thermochromism is evidently not a simple function of the isolated molecule, and an explanation of it must take into account the special conditions which exist in the solid.

Ubbelohde and Gallagher [16] have discussed hydrogen bonds in crystals from the point of view of the modern theory of acids and bases. These authors conclude that " proton-transfer defect sites "—sites where the protons are in the " wrong " positions on hydrogen bonds—should occur quite generally in such crystals, the extent depending on the relative energies of the normal and the defect positions, and on the temperature. The thermochromism of the methylene-bridged compounds which have been considered here can be discussed along similar lines. At absolute zero all the molecules in the crystals are in the lactim state; as the temperature rises, " defects " appear in the crystals in the form of lactam molecules resulting from the co-operative transfer of pairs of protons across the internal hydrogen bonds; since the lactam form absorbs light at a longer wavelength, the crystals become more deeply coloured. The tautomeric nature of the methylene-bridged compounds provides them with an additional means of absorbing energy, which is effective in the solid because it does not require any substantial movement or change in the overall shape of the molecules.

Experimental

Symmetrical Thermochromic Compounds from Heterocyclic Phenols and Formaldehyde.—2-Hydroxyacridine (3 g.) and anhydrous sodium acetate (2 g.) were added to alcohol (50 ml.), and the mixture warmed to the b. p. 40% Aqueous formaldehyde (25 ml.) was added and the mixture refluxed for 10 min. The resulting red precipitate of *1,1′-methylenedi-2-hydroxyacridine* was separated by filtration, washed with water, and dried (2·8 g.). Recrystallisation gave orange needles from chloroform or red prisms from dioxan; both forms had m. p. 350° (decomp.) (Found: C, 80·8; H, 4·7; N, 7·0. $C_{27}H_{18}N_2O_2$ requires C, 80·6; H, 4·5; N, 7·0%). The *diacetyl derivative*, formed by refluxing acetic anhydride and sodium acetate, was pale yellow (from dioxan) with m. p. 263—265° (Found: C, 76·7; H, 4·45; N, 5·85. $C_{31}H_{22}N_2O_4$ requires C, 76·5; H, 4·6; N, 5·8%).

2-Hydroxy-5-phenylacridine reacted with formaldehyde under the above conditions, to give *1,1′-methylenedi-(2-hydroxy-5-phenylacridine)*, pale orange needles (from benzene) or red prisms (from dioxan), m. p. (both forms) 333—335° (decomp.) (Found: C, 84·8; H, 4·8; N, 4·6. $C_{39}H_{26}N_2O_2$ requires C, 84·5; H, 4·7; N, 5·1%).

2-Hydroxyphenazine gave *1,1′-methylenedi-2-hydroxyphenazine*, yellow needles (from chlorobenzene), m. p. 331—334° (decomp.) (Found: C, 74·6; H, 4·1; N, 13·3. $C_{25}H_{16}N_4O_2$ requires C, 74·2; H, 4·0; N, 13·9%).

2-Hydroxy-3,4-dimethylphenazine gave *1,1′-methylene-di-(2-hydroxy-3,4-dimethylphenazine)*, yellow needles (rapid crystallisation from toluene) or brick-orange prisms (slow crystallisation from toluene), m. p. (both forms) 350° (decomp.) (Found: C, 75·4; H, 5·2; N, 12·3. $C_{29}H_{24}N_4O_2$ requires C, 75·6; H, 5·25; N, 12·2%). The general procedure of John [14] for the preparation of 2-hydroxy-1,3,4-trimethylphenazine was followed in preparing the 3,4-dimethyl compound except that Thiele's original conditions [17] were used to form 1,2,4-triacetoxy-5,6-dimethylbenzene from *o*-xyloquinone. The final condensation of hydroxyxyloquinone with *o*-phenylenediamine was carried out under the conditions described by Kehrmann and Cherpillod [18] for the preparation of 2-hydroxyphenazine: yields were improved with an excess of the diamine.

Unsymmetrical Thermochromic Compounds.—2-Hydroxyacridine (5 g.), dimedone (10 g.), and sodium acetate (5 g.) were warmed in alcohol (250 ml.) on a water-bath. 40% Aqueous formaldehyde (50 ml.) was then added. After a minute the 2-hydroxyacridine had dissolved and a deep red colour had developed. The solution was heated under reflux for 10 min., then poured into cold water (2 l.) and left for 15 min. The red solid was separated, washed with water, dried, dissolved in benzene (200 ml.) and placed on a short alumina column. A solution of 1 : 99 alcohol–benzene was used for elution and the first deep red band taken. The volume of this fraction was reduced to 30 ml. and the solution left to crystallise. This gave *1-(4,4-dimethyl-2,6-dioxocyclohexylmethyl)-2-hydroxyacridine* (4·5 g., 50%), m. p. 200—202°. Recrystallisation from benzene gave large red prisms (3·4 g.), m. p. 202—203° (Found: C, 76·0; H, 5·8; N, 4·2. $C_{22}H_{21}NO_3$ requires C, 76·1; H, 6·1; N, 4·0%).

[16] Ubbelohde and Gallagher, *Acta Cryst.*, 1955, **8**, 71.
[17] Thiele, *Ber.*, 1898, **31**, 1247.
[18] Kehrmann and Cherpillod, *Helv. Chim. Acta*, 1924, **7**, 973.

XUM

Under similar conditions 2-hydroxy-3,4-dimethylphenazine gave 1-(*4,4-dimethyl-2,6-dioxocyclohexylmethyl*)-*2-hydroxy-3,4-dimethylphenazine*. This crystallised from toluene as yellow needles, m. p. 219°, which changed slowly into dark brown prisms. Brown crystals, m. p. 219°, were obtained directly from benzene (Found: C, 73·6; H, 6·3; N, 7·5. $C_{23}H_{24}N_2O_3$ requires C, 73·4; H, 6·4; N, 7·4%).

1-Formyl-2-hydroxyacridine.—Aqueous sodium hydroxide (4 g. in 10 ml. of water) was added to a suspension of 2-hydroxyacridine (2 g.) in alcohol (20 ml.). Chloroform (2 ml.) was added during 10 min., the temperature being kept just below the b. p. during the addition and for a further hour. The mixture was then heated under reflux for 1½ hr. and the excess of chloroform and most of the alcohol were removed under reduced pressure. The solid was separated, suspended in water, and acidified with hydrochloric acid. The mixture was warmed slightly and filtered to remove tar. The filtrate was neutralised with sodium hydrogen carbonate, and the resulting yellow precipitate of *1-formyl-2-hydroxyacridine* recrystallised twice from water, giving yellow needles (0·4 g., 20%), m. p. 232—233° (Found: C, 75·1; H, 4·0; N, 6·1. $C_{14}H_9NO_2$ requires C, 75·3; H, 4·1; N, 6·3%). Attempts to oxidise the aldehyde to the acid were unsuccessful: with boiling nitric acid there was little effect on the aldehyde; on aerial oxidation of a hot alkaline solution a complex mixture was formed (paper chromatography with ethyl methyl ketone–water as solvent was used to detect oxidation products).

Spectra.—Ultraviolet and visible absorption spectra (see Tables) were determined with a Unicam quartz spectrophotometer (S.P. 500).

Maxima and shoulders (sh) (mμ) *in ultraviolet and visible absorption spectra of* 1,1′*-methylenedi-2-hydroxyacridine.*

				In 9 : 1 *cyclohexane–chloroform*						
λ	236	264	298sh	324sh	337	355	402	—	490sh	—
log ε	4·72	5·12	3·94	3·74	4·04	4·32	3·88	—	2·68	—
				In chloroform						
λ	—	265	299	—	338	355	398	434sh	490	530sh
log ε	—	5·04	4·34	—	4·06	4·32	3·82	3·64	3·50	3·16
				In absolute alcohol						
λ	235	262	290	—	348sh	355	400sh	—	472	515sh

Maxima and shoulders (sh) (mμ) *in ultraviolet and visible absorption spectra of* 1-(*4,4-dimethyl-2,6-dioxocyclohexylmethyl*)-*2-hydroxyacridine.*

				In cyclohexane					
λ	236	260	292sh	322sh	338	355	406	518	545sh
log ε ...	4·50	4·86	3·78	3·38	3·72	3·92	3·60	2·58	2·44
				In absolute alcohol					
λ	235	260	—	—	352sh	364	420sh	480	—
log ε ...	4·46	4·74	—	—	3·98	4·10	3·40	3·54	—
				In 10% *aqueous-alcohol*					
λ	236	265	298sh	—	352sh	364	—	445	—
log ε ...	4·32	4·80	3·94	—	4·04	4·20	—	3·56	—

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Edinburgh, 9.

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35. *The 4-Hydroxypipecolic Acid from* Acacia *species, and its Stereoisomers.*

By J. W. Clark-Lewis and P. I. Mortimer.

4-Hydroxypipecolic acid has been isolated on a preparative scale from *Acacia oswaldii* leaves and separated from accompanying acids through the ether-soluble *N*-nitroso-acid. Hydrolysis of this derivative and separation on an ion-exchange column gave (−)-pipecolic acid and the hydroxy-acid, which was shown by unequivocal degradations to be (−)-*trans*-4-hydroxy-L-pipecolic acid. This acid has been converted by stereospecific transformations into *cis*-4-hydroxy-L- and -D-pipecolic acid, so that three of the four optically active forms of 4-hydroxypipecolic acid are now available.

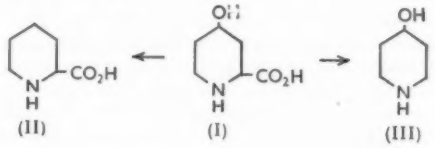
4-Hydroxypipecolic acid (I) was first isolated in 1955 by Virtanen and Kari [1] from some *Acacia* species and subsequent reports concern its structure [2,3,4] and isolation from other sources, *e.g.*, *Armeria* species,[2,3] heartwood of *Acacia excelsa*, and heartwood and sapwood of *A. mollissima*.[4] *Acacia oswaldii* leaves [4] offer a convenient source from which the acid has been isolated in 20—25 g. batches, and it is here free from the better known 5-hydroxypipecolic acid.[5,6] The leaves were extracted with 80% ethanol; the total nitrogenous acids (1·65%) were isolated on an ion-exchange column, and imino-acids were separated from amino-acids through the *N*-nitroso-derivatives as described for 5-hydroxypipecolic acid by Witkop and Foltz,[6] and again purified on an ion-exchange column. This gave (−)-pipecolic acid and a product, $C_6H_{11}O_3N$, melting at 294° (decomp.), 24° above the recorded [1] m. p. of 4-hydroxypipecolic acid. The latter product was characterised by various new derivatives; the ready cyclisation of the 1-phenylcarbamoyl compound to a hydantoin derivative revealed the α-imino-acid structure. This was confirmed by reduction of the natural acid with hydriodic acid and red phosphorus to pipecolic acid (II) (16%), the reduction being accompanied by racemisation as in the case of hydroxyproline.[7] When heated with aqueous barium hydroxide the natural acid was partially epimerised, and the new product was chromatographically indistinguishable from synthetic *cis*-4-hydroxypipecolic acid supplied by Dr. Vanderhaeghe. The synthetic acid was similarly epimerised to a mixture of *cis*- and *trans*-acids, and both these were distinguishable from 3- [8] and 5-hydroxypipecolic acid [6] by paper chromatography.[4] The position of the hydroxyl group in 4-hydroxypipecolic acid was then confirmed by decarboxylation of the acid in acetophenone by the method introduced by Chatelus.[9] This gave dimorphic 4-hydroxypiperidine (III) smoothly, but in lower yield (37%) than reported for decarboxylation of acyclic amino-acids,[9] and this completed the chemical proof of the 4-hydroxypipecolic acid structure (I).

The *trans*-configuration (IV) was indicated by the compound's differing chromatographically from *cis*-4-hydroxypipecolic acid prepared by hydrogenation of 4-hydroxypicolinic acid. Moreover the higher R_F value of the *trans*- than of the *cis*-acid agreed with the assumed conformations (2-*eq*,4-*ax* and 2-*eq*,4-*eq* respectively), and the acid and its derivatives showed no tendency to lactonise. (−)-*trans*-4-Hydroxypipecolic acid belongs to the L-series of imino-acids, as was expected from its occurrence with (−)-L-pipecolic acid and confirmed by its less negative rotation in aqueous hydrochloric acid than in water.

[1] Virtanen and Kari, *Acta Chem. Scand.*, 1955, **9**, 170.
[2] Fowden, *Biochem. J.*, 1958, **70**, 629.
[3] Virtanen and Gmelin, *Acta Chem. Scand.*, 1959, **13**, 1244.
[4] Clark-Lewis and Mortimer, *Nature*, 1959, **184**, 1234.
[5] Virtanen and Kari, *Acta Chem. Scand.*, 1954, **8**, 1290; Grobbelaar, Pollard, and Steward, *Nature*, 1955, **175**, 703.
[6] Witkop and Foltz, *J. Amer. Chem. Soc.*, 1957, **79**, 192.
[7] Fischer, *Ber.*, 1902, **35**, 2660.
[8] Plieninger and Leonhäuser, *Chem. Ber.*, 1959, **92**, 1579.
[9] Chatelus, *Compt. rend.*, 1959, **248**, 690.

XUM

The acid thus conforms to Lutz and Jirgensons's empirical rule[10,11] that protonation of the carboxyl group in the L-series causes a decrease in the negative rotation (rotation becomes more positive, see Table); the validity and scope of this rule have been examined,[11] and it has proved useful with 5-hydroxypipecolic acid.[6] A further regularity apparent from the

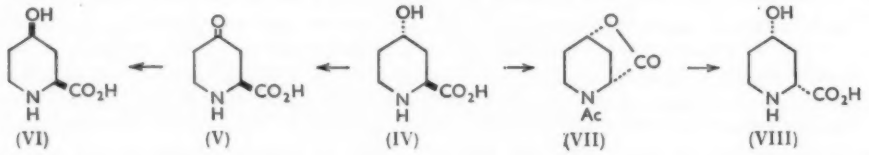


(II) (I) (III)

Table is that the change in molecular rotation is greater in the *cis*- than in the *trans*-series, which supports the assignment to the natural acid of the (—)-*trans*-4-hydroxy-L-pipecolic acid structure with the absolute configuration shown (IV).

Acids of L-series	$[M]_D$ in H_2O	$[M]_D$ in H_2O with 1 equiv. of mineral acid	$[M]_D$ in 5N-HCl	$[M]_D$ in acid minus $[M]_D$ in H_2O
Proline [10b]	−100°	−71°	—	+29°
Hydroxyproline [11]	−100	—	−66°	+34
cis-4-Hydroxyproline	−78	—	−25	+53
Pipecolic	−33	—	−14	+19
trans-4-Hydroxypipecolic	−19	—	+4	+23
cis-4-Hydroxypipecolic	−28	—	+11	+39
trans-5-Hydroxypipecolic [6]	−34	−20	—	+14
cis-5-Hydroxypipecolic [6]	−45	−17	—	+28

The *trans*-L-configuration (IV) was then substantiated by transformation of the (—)-4-hydroxypipecolic acid *via* the keto-L-acid (V) into (—)-*cis*-4-hydroxy-L-pipecolic acid (VI), and *via* the *N*-acetyl-lactone (VII) into (+)-*cis*-4-hydroxy-D-pipecolic acid (VIII). The



(VI) (V) (IV) (VII) (VIII)

keto-acid (V) formed by oxidation of the 4(*ax*)-hydroxy-2(*eq*)-carboxylic acid (IV) was expected to retain the 2(*eq*)-conformation, and reduction of the unhindered carbonyl group by sodium borohydride then gave predominantly the expected[12] 4(*eq*)-hydroxy-2(*eq*)-carboxylic acid, *viz.* (—)-*cis*-4-hydroxy-L-pipecolic acid (VI), chromatographically identical with the synthetic *cis*-acid. Oxidation was effected with the unacylated imino-acid (IV) so that paper chromatography could be used as an aid in determining the conditions for both oxidation (with chromic acid) and isolation of products, and in this way the keto-acid (V) was obtained in 36% yield and β-alanine, the only other ninhydrin-positive oxidation product, was isolated as the *N*-phenylcarbamoyl derivative (2·2%). 4-Oxo-L-pipecolic acid (V) was found to be stable in acid solution and decomposed only slowly in neutral or in alkaline solution, in marked contrast to the behaviour of 4-oxoproline,[13] 5-oxopipecolic acid,[14] and *N*-benzyloxycarbonyl-5-oxopipecolic acid.[6] Moreover the stability of the acid precludes a β-keto-acid structure and thus provides independent confirmation of the location of the carboxyl group.

[10] Lutz and Jirgensons, *Ber.*, (*a*) 1930, **63**, 448, (*b*) 1931, **64**, 1221.
[11] Winitz, Birnbaum, and Greenstein, *J. Amer. Chem. Soc.*, 1955, **77**, 716.
[12] Barton, *J.*, 1953, 1027; Dauben, Fonken, and Noyce, *J. Amer. Chem. Soc.*, 1956, **78**, 2579.
[13] Patchett and Witkop, *J. Amer. Chem. Soc.*, 1957, **79**, 185.
[14] King, King, and Warwick, *J.*, 1950, 3590.

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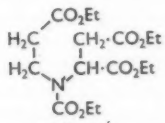
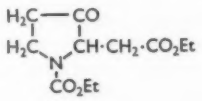
The disposition of hydroxyl and carboxyl groups in (−)-*trans*-4-hydroxy-L-pipecolic acid (IV) is unfavourable for lactone formation, but the acid suffered inversion at the 2-position with formation of the *N*-acetyl-D-lactone (VII) when boiled with acetic anhydride in acetic acid. Hydrolysis of the lactone then gave (+)-*cis*-4-hydroxy-D-pipecolic acid (VIII), enantiomorphous with (−)-cis-L-acid (VI) obtained by reduction of the keto-acid with sodium borohydride. Racemisation at the α-carbon atom in *N*-acyl-α-amino-acids on treatment with acetic anhydride is well known and was used to epimerise hydroxyproline;[15] it is usually held to proceed through an oxazolone (see, *e.g.*, footnote 15, ref. 6), although this clearly is not so in the case of phthaloyl-L-glutamic anhydride which is similarly racemised.[16] Inversion at the 2-carbon atom is confirmed in the present case by application of Hudson's lactone rule:[17] $[M]_D$ of the lactone (VII) is +306° (1% in ethanol) and is more positive by 208° than $[M]_D$ +98° (1% in ethanol) of the *N*-benzoyl (in lieu of *N*-acetyl) derivative of the acid (VIII) (rotation measured with the enantiomorph, VI). A mixture of the *trans*-L- and the *cis*-D-acid was formed by partial inversion at the 2-position when the L-acid was heated with aqueous barium hydroxide or when *trans*-*N*-benzoyl-4-hydroxy-L-pipecolic acid was heated above its m. p. and then hydrolysed. Crystallisation of the copper salts gave a series of fractions each containing approximately equal amounts of *cis*- and *trans*-salt so that this method, which proved so effective with the epimeric hydroxyprolines,[18] could not be used to separate *cis*- and *trans*-4-hydroxypipecolic acid.

Synthesis of (±)-*cis*-4-hydroxypipecolic acid by catalytic hydrogenation of 4-hydroxypicolinic acid was achieved in very low yield by us (1·4% isolated as the hydrochloride) and by Fowden.[2] Yields were not improved by using newly prepared 4-benzyloxypicolinic acid because catalytic hydrogenation led first to 4-hydroxypicolinic acid through hydrogenolysis of the benzyl group. An alternative synthesis was therefore attempted by condensing *N*-ethoxycarbonyl-β-alanine ethyl ester with diethyl fumarate, giving the ester (IX), in the hope that Dieckmann cyclisation would yield a piperidone derivative. Cyclisation, however, gave a pyrrolidone which on hydrolysis, decarboxylation of the β-keto-acid, and re-esterification gave the keto-ester (X). Reduction of the keto-ester by sodium borohydride and hydrolysis then gave 3-hydroxypyrrolidine-2-acetic acid (XI).


(IX)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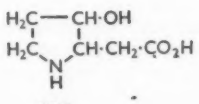
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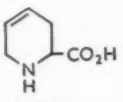
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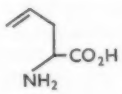
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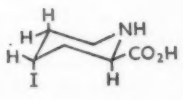
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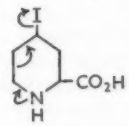
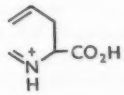

(XV)


(XVI)

Paper chromatography greatly aided this investigation and all structural features of *trans*-4-hydroxypipecolic acid (IV) except the absolute configuration were in fact known from application of this analytical technique to reactions effected on a few milligrams of material, before being confirmed by isolation of products or by alternative degradations. A particularly interesting, and at first puzzling, series of observations was made on the reduction of the acid with hydriodic acid. This gave pipecolic acid, as already noted, and

[15] Robinson and Greenstein, *J. Biol. Chem.*, 1952, **195**, 383.
[16] Jackson, Thesis, Nottingham, 1951.
[17] Witkop, *Experientia*, 1956, **12**, 372.
[18] (*a*) Leuchs and Felser, *Ber.*, 1908, **41**, 1726; (*b*) Wieland and Wintermeyer, *Chem. Ber.*, 1957, **90**, 1721.

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two other ninhydrin-positive components regarded as iodo-derivatives (cf. hydroxyproline [18a]) which were also observed by Virtanen and Kari [1] and by Fowden.[2] Although unchanged in R_F after addition of ammonia, both disappeared when the reduction mixture was treated with silver carbonate and instead there appeared baikiain [14] (XII) and 2-aminopent-4-enoic acid (XIII). The former was chromatographically indistinguishable from natural baikiain, and the latter was recognised on hydrogenation of the silver-treated reduction mixture to 2-aminopentanoic acid (norvaline); the identification was then confirmed by paper-chromatographic comparison with synthetic material (XIII). Baikiain, pipecolic acid, α-aminopent-4-enoic acid, and norvaline give characteristically different colours with spray reagents, and this aided identification. It seems clear that the iodo-compounds, possessing different R_F values, are epimeric 4-iodopipecolic acids with iodine in 4(*ax*)- (XIV) and 4(*eq*)-orientation. *trans*-Elimination of hydrogen iodide from the former (XIV) accounts for the formation of baikiain, the preferential elimination of the 5- instead of the 3-hydrogen atom apparently being controlled by the carboxyl group (or ion). The iodine in the epimer (XV) is unfavourably placed for *trans*-1,2-elimination with hydrogen, but movement of the electrons of the 5,6-bond initiated by development of a 4-carbonium ion, and assisted by the nitrogen lone-pair electrons, would lead to the precursor (XVI) of 2-aminopent-4-enoic acid. A similar elimination with loss of a ring-carbon atom is entailed in the conversion of quinine into niquine,[19] and a close analogy is provided by the ring fission which occurs when 3β-chlorotropane (but not the 3α-isomer) is treated with potassium cyanide.[20]

Experimental

Paper chromatograms were run with butan-1-ol–acetic acid–water (4 : 1 : 5) [21] except where otherwise indicated. Distances from the origin are quoted instead of R_F values in cases where the solvent was allowed to drip from the paper.

Materials.—*Acacia mollissima* was supplied by the South Australian Woods and Forests Department, and *A. excelsa* (herbarium specimen numbers 55 and 890) was obtained by courtesy of the Chemical Research Laboratories, C.S.I.R.O. *A. oswaldii* leaves were collected locally in the River Murray valley.

Isolation of Imino-acids.—(a) *From leaves.* The extractive obtained from undried *Acacia oswaldii* leaves (5·5 kg.) with 80% ethanol was dissolved in water and transferred in two portions to a column of sulphonated polystyrene (Zeokarb 225; 970 g.) and the amino-acids (95 g.) were eluted with 3N-ammonia. The imino-acids were extracted into ether as the *N*-nitroso-derivatives, as described for 5-hydroxypipecolic acid; [6] 2N-hydrochloric acid was placed in the receiver during the continuous ether-extraction to avoid rapid decomposition of the *N*-nitroso-compounds during evaporation of ether from the extract; the ether extract also contained much oxalic acid. The acidic solution of *N*-nitroso-compounds was boiled and evaporated, and the imino-acids were recovered by absorption on ZeoKarb 225 and elution with 3N-ammonia. The imino-acids (46 g.) were dissolved in boiling water (58 c.c.), and the hot solution was diluted with boiling ethanol, which caused separation of a brown deposit and slower crystallisation of 4-hydroxpipecolic acid. A solution of the crude product (20·7 g.) in water (500 c.c.) containing acetic acid (2·5 c.c.) deposited most of the brown pigment when stored at 0°, and the filtrate was completely decolorised by filtration through charcoal (2 g.) mixed with kieselguhr. The solution was evaporated and crystallisation of the residue from aqueous ethanol gave *trans*-4-hydroxy-L-pipecolic acid (17·8 g.), m. p. 285—286° (decomp.). Concentration of mother-liquors from the first crop (20·7 g.) and purification of the residue (6·9 g.) in the same way gave a further 5·2 g. (total 23 g., 0·4%), m. p. 287° (decomp.).

L-Pipecolic acid was obtained as the hydrochloride by evaporation of hydrochloric acid with the mother-liquors from the isolation of 4-hydroxypipecolic acid, and from the aqueous solution

[19] Turner and Woodward, in Manske and Holmes, "The Alkaloids," Academic Press, New York, 1953, Vol. III, p. 21—22.
[20] Archer, Lewis, and Zenitz, *J. Amer. Chem. Soc.*, 1958, **80**, 958; Archer, Bell, Lewis, Schulenberg, and Unser, *ibid.*, p. 4677.
[21] Partridge, *Biochem. J.*, 1948, **42**, 238.

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remaining after ether-extraction of the *N*-nitroso-compounds by evaporation and extraction of the residue with ethanol. Crystallisation from aqueous ethanol gave (−)-pipecolic acid hydrochloride (6·5 g. from 17·3 kg. of leaves), m. p. 256—258°, $[\alpha]_D^{18}$ −10·5° (8% in H_2O).

Separation of 4-hydroxypipecolic acid and pipecolic acid was also achieved by selective elution from ZeoKarb 225, and the former was eluted with 0·2—0·4N-hydrochloric acid, while the latter (and proline) required 0·4—0·8N-acid. The mother-liquors from the isolation of 4-hydroxypipecolic acid from 20 kg. of leaves were treated in this way, and the column was finally washed with 1·6N-hydrochloric acid before elution with aqueous ammonia gave a *compound* (1·66 g.) crystallising from aqueous ethanol in needles (1·5 g.), m. p. 231—234° (decomp.), $[\alpha]_D^{24}$ +15° (1% in H_2O), $[\alpha]_D^{26}$ +22° (1% in 5N-HCl) [Found: C, 46·7; H, 7·8; N, 13·1. $(C_4H_9O_2N)_2$ requires C, 47·05; H, 7·9; N, 13·7%]. When chromatographed for 30 hr. the compound moved 10 cm. compared with pipecolic acid (23·5 cm.), *trans*-4-hydroxypipecolic acid (15·8 cm.), and *cis*-4-hydroxypipecolic acid (12·9 cm.). It gave a reddish-grey colour (red fluorescence under ultraviolet light) with ninhydrin at 100° and a green colour with isatin at 100°. A solution in 6N-hydrochloric acid was boiled for 16 hr., but no other ninhydrin-positive component was then found in the solution.

(b) *From* Acacia *sp. heartwoods and sapwoods.* Milled heartwood of *A. excelsa* (2094 g.) was extracted with light petroleum (b. p. 60—80°) for 12 hr. (1·8 g. of yellow waxy extractive), ether for 34 hr. (7·4 g. of extractive), acetone for 7 hr. (34 g. of extractive) and ethanol for 8 hr. Concentration of the ethanolic extract left a viscous residue (73 g.) which was diluted with water and filtered from an amorphous brown deposit. The filtrate was extracted with ethyl acetate for three periods of 8 hr. and the residue (20·7 g.) remaining from evaporation of the aqueous phase was dissolved in water (10 c.c.) which was then diluted with ethanol (100 c.c.). Crystallisation gave a mixture (9·85 g.) of 4-hydroxypipecolic and pipecolic acid contaminated with amorphous brown impurity. The mother-liquors and the crude imino-acid fraction were separately boiled with 6N-hydrochloric acid for 24 hr. to precipitate polyphenolic material, and the imino-acids were collected on a cation-exchange resin and eluted with 0·5N-ammonia. Evaporation of the eluates and repeated crystallisation of the residue from aqueous ethanol gave *trans*-4-hydroxypipecolic acid in colourless prisms (*ca.* 4·0 g., 0·19%), m. p. 294° (decomp.). The concentrated mother-liquors (2 g.) in water (4 c.c.) were chromatographed on Whatman 3 MM paper (7 sheets, each 25 cm. wide). (−)-Pipecolic acid (0·35 g., 0·017%), m. p. 273—275° (decomp.), $[\alpha]_D^{23}$ −25° (2% in H_2O), was extracted with boiling ethanol from appropriately dissected areas of the papers. 4-Hydroxypipecolic acid, similarly extracted from the chromatograms, failed to crystallise.

Similar extractions of other samples of *A. excelsa* heartwood gave crystalline 4-hydroxypipecolic acid (0·017—0·08%) and pipecolic acid (0·001—0·01%). 4-Hydroxypipecolic acid (0·01—0·03%) was also obtained from *A. mollissima* heartwood and sapwood.

(−)-trans-4-*Hydroxy-*L*-pipecolic Acid.*—The acid isolated as described above was obtained in clusters of prisms, m. p. 294° (decomp.) [lit.,[1] 270° (decomp.)], by repeated crystallisation from aqueous ethanol (Found, on material dried at 90° *in vacuo* over P_2O_5 for 1½ hr.: C, 49·7; H, 7·7; N, 9·8; *C*-Me, 0·1; OMe, 0·4. Calc. for $C_6H_{11}O_3N$: C, 49·6; H, 7·6; N, 9·65%). Samples isolated from three different batches had $[\alpha]_D^{20}$ −13° ± 0·4° (1% in H_2O); the acid has $[\alpha]_D^{16}$ +2·7° (1% in 5N-HCl) and $[\alpha]_D^{25}$ −6·0° (1% in N-NaOH). Virtanen and Gmelin [3] record $[\alpha]_D^{21}$ −12·5° (in H_2O) +0·34° (in N-HCl), and −18·5° (in N-NaOH). The acid did not react with periodic acid at a significant rate under the many conditions tested. The 1-(2,4-*dinitrophenyl*) *derivative* prepared by the general method [22] crystallised from aqueous ethanol in orange prisms, m. p. 183° (Found: C, 46·1; H, 4·2; N, 13·6. $C_{12}H_{13}O_7N_3$ requires C, 46·3; H, 4·2; N, 13·5%). 4-Hydroxypipecolic acid hydrochloride failed to crystallise. The *copper salt* crystallised from a concentrated aqueous solution (solubility *ca.* 1 in 2 at 100° and *ca.* 1 in 7 at room temperature) during 3 days in deep blue prisms, m. p. 229° (decomp.) (Found, on an air-dried sample: N, 6·5; CuO, 17·2; loss on drying at 90°, 16·2. $C_{12}H_{20}O_6N_2Cu,4H_2O$ requires N, 6·6; CuO, 18·7; H_2O, 17·0%). 4-Hydroxypipecolic acid on paper chromatograms sprayed with ninhydrin and heated at 100—110° for 5—10 min. gave a dull colour ranging from greyish-green to brownish-purple, with a dull red fluorescence in ultraviolet light, and with isatin under similar conditions it gave a green colour. The colours developed by the sprayed papers were found to vary markedly with the drying temperature. Thus at 80° isatin gave no colour, at 100° a faint purple, and at 115° a purple colour; these two colours became green during 24 hr. at room temperature. With

[22] Rao and Sober, *J. Amer. Chem. Soc.*, 1954, **76**, 1328.

ninhydrin, heated at 80°, the initial yellow-brown colour became greyish-purple after 15 min. at room temperature.

(−)-trans-1-*Benzoyl*-4-*hydroxy*-L-*pipecolic Acid*.—The *benzoyl derivative* (60—70%) was prepared by Schotten–Baumann benzoylation at 0° and crystallised from aqueous ethanol in stout needles, m. p. 174°, $[\alpha]_D^{15}$ −54° (1% in EtOH) (Found: C, 62·8; H, 6·1; N, 5·6. $C_{13}H_{15}O_4N$ requires C, 62·6; H, 6·1; N, 5·6%). Recrystallisations from aqueous ethanol gave a poor recovery unless allowed to proceed at 0° for several days, and it was advantageous to remove as much ethanol as possible by boiling the solution after dilution. Benzoylation with an excess of benzoyl chloride did not yield the dibenzoate; heating the 1-benzoyl derivative above its m. p. caused epimerisation at the 2-carbon atom (see below).

(−)-trans-4-*Hydroxy*-1-*toluene*-p-*sulphonyl*-L-*pipecolic Acid*.—Toluene-*p*-sulphonyl chloride (0·95 g., 1·2 equiv.) in acetone (5 c.c.) was added to a solution of 4-hydroxypipecolic acid (0·58 g.) in water (5 c.c.) and 10N-sodium hydroxide (1·2 c.c.). The mixture was shaken for 15 min. before acidification with 10N-hydrochloric acid (1 c.c.), and was then extracted with ethyl acetate. The dried (Na_2SO_4) extract was concentrated, and re-evaporated after addition of benzene. Crystallisation gave (−)-trans-4-*hydroxy*-1-*toluene*-p-*sulphonyl*-L-*pipecolic acid* (0·7 g., 58%), m. p. 153—154° raised to m. p. 162° by recrystallisation (prisms) from ethyl acetate–benzene, $[\alpha]_D^{19}$ −16° (1% in EtOH) (Found: C, 51·8; H, 5·5; N, 4·5; S, 10·7. $C_{13}H_{17}O_5NS$ requires C, 52·1; H, 5·7; N, 4·7; S, 10·7%).

(−)-trans-4-*Hydroxy*-1-*phenylcarbamoyl*-L-*pipecolic Acid and* (−)-trans-4′-*Hydroxy*-3-*phenyl-piperidino*(1′,2′:1,5)-*hydantoin*.—Phenyl isocyanate (0·6 g., 1·25 equiv.) was added in portions with shaking during 10 min. to a cold solution of 4-hydroxypipecolic acid (0·58 g.) in N-sodium hydroxide (4 c.c.). Diphenylurea was precipitated after the last addition, and acidification gave an oil which solidified (0·72 g., 68%). Reprecipitation by acidification of a cold solution in aqueous 2—3% sodium carbonate gave the *phenylurea* (0·48 g.), m. p. 181—197° after sintering at 176°, $[\alpha]_D^{26}$ −24·5° (1% in EtOH) unchanged after 24 hr. (Found: C, 59·0; H, 6·2; N, 10·5. $C_{13}H_{16}O_4N_2$ requires C, 59·1; H, 6·1; N, 10·6%). The phenylurea (1·49 g.) was dissolved in boiling water, and the filtered solution was concentrated (to 53 g.). Crystallisation gave the *piperidinohydantoin* in prisms (1·05 g.), m. p. 204—205°, $[\alpha]_D^{23}$ −53° (1% in EtOH) (Found: C, 63·5; H, 5·6; N, 11·5. $C_{13}H_{14}O_3N_2$ requires C, 63·4; H, 5·7; N, 11·4%). The hydantoin showed hydroxyl absorption at 2·88 μ and carbonyl absorption at 5·63 and 5·85 μ (Nujol; calcium fluoride prism). The hydantoin (0·61 g.) dissolved slowly (*ca.* 1 hr.) in N-sodium hydroxide (4·63 c.c.), and the solution after dilution to 10 c.c. then had $[\alpha]_D$ −17°, $[\alpha]_D$ −40° after 3 hr., and $[\alpha]_D$ −45·4° (6·1% in 2 equiv. of aqueous sodium hydroxide) after 24 hr. and after 48 hr. A solution of the hydantoin (0·1 g.) in N-sodium hydroxide (10 c.c.) was both prepared and kept at 25°, and optical rotations of the solution were observed at intervals measured from the first contact with alkali: $[\alpha]_D^{25}$ −17° after 1 hr., −30° (1½ hr.), −32·5° (2 hr.), −42° (3½ hr.), −43° (6½ hr.), and −43·5° (23 hr.). The acidified solution slowly deposited the hydantoin (0·047 g.), m. p. and mixed m. p. 205—206°.

(−)-trans-3-*Phenyl*-4′-*phenylthiocarbamoyloxypiperidino*(1′,2′:1,5)-2-*thiohydantoin*.—The derivative was prepared by Edman's method [23] but at room temperature: [24] 4-Hydroxypipecolic acid (0·725 g.) in 50% aqueous pyridine (25 c.c.) was adjusted to pH 10·0 with N-sodium hydroxide (1·4 c.c.), phenyl isothiocyanate (1·2 c.c.) was added, and the mixture was shaken vigorously. Aqueous sodium hydroxide was added as required (during the first 15 min.) to maintain pH 9·0. The alkaline solution was extracted with benzene, and the aqueous layer filtered through kieselguhr before acidification with 1·25N-hydrochloric acid. The granular yellow precipitate was collected, washed with water, suspended in 2N-hydrochloric acid (15 c.c.), and boiled for 2 hr. before evaporation to dryness under reduced pressure. Crystallisation from aqueous acetic acid gave the *thiohydantoin* (0·56 g., 28%), m. p. 201—202° raised by recrystallisation from ethanol (yellow plates) (0·45 g.) to 213—214° and then 214°, $[\alpha]_D^{23}$ −74° (0·2% in EtOH) (Found: C, 60·5; H, 4·9; N, 9·6; S, 15·6. $C_{20}H_{19}O_2N_3S_2$ requires C, 60·4; H, 4·8; N, 10·6; S, 16·1%).

Reduction of 4-*Hydroxypipecolic Acid by Hydriodic Acid*.—(a) *Isolation of pipecolic acid*. 4-Hydroxypipecolic acid (0·051 g.), red phosphorus (0·023 g.), and hydriodic acid (*d* 1·94; 1 c.c.) were heated in a sealed tube at 145° for 6 hr. and the colourless solution was evaporated under reduced pressure. Pipecolic acid (0·0076 g., 16%) was detected and estimated by

[23] Edman, *Acta Chem. Scand.*, 1950, **4**, 277.
[24] Ingram, *J.*, 1953, 3717.

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quantitative paper chromatography (R_F 0·37). 4-Hydroxypipecolic acid (2 g.), red phosphorus (0·32 g.), and hydriodic acid (*d* 1·94; 20 c.c.) were heated in four sealed tubes at 150° for 12 hr. The solutions were combined and found to contain pipecolic acid (R_F 0·37) and components with R_F 0·48 and 0·56 (run for 12 hr.; solvent front moved 24 cm.). The solution was evaporated to remove hydriodic acid and the passed through a ZeoKarb 225 column (50 g.). Elution with ammonia gave pipecolic acid and several components of lower R_F; imino-acids were separated through their *N*-nitroso-derivatives which, after hydrolysis and passage through a ZeoKarb 225 column, gave imino-acids (0·77 g.) consisting of pipecolic acid and traces of other ninhydrin-positive substances. The mixture failed to crystallise and was therefore transferred to a ZeoKarb 225 column and eluted successively with 0·5N-hydrochloric acid (500 c.c.), N-hydrochloric acid (250 c.c.), water (500 c.c.), and 2N-ammonia (500 c.c.). The eluted fractions (*ca.* 70 c.c. each) were evaporated and examined by paper chromatography. Pipecolic acid was present in the later 0·5N-hydrochloric acid eluates, those with N-acid, and the first ammonia eluates. Fractions containing other ninhydrin-positive substances in addition to pipecolic acid were returned to the column and eluted with acid of more gradually increased strength. Combined pipecolic acid fractions were evaporated to dryness under reduced pressure, and recrystallisation of the residues from ethanol gave pipecolic acid hydrochloride (0·22 g., 8·5%), m. p. and mixed m. p. 256—258°, $[\alpha]_D$ −0·3° (6% in H_2O).

(b) *Formation of baikiain and 2-aminopent-4-enoic acid.* 4-Hydroxypipecolic acid (0·02 g.), red phosphorus (0·007 g.), and hydriodic acid (*d* 1·94; 0·2 c.c.) were heated at 145° for 12 hr. and the colourless solution was evaporated to dryness under reduced pressure. The residue was dissolved in water (2 c.c.) and examined by paper chromatography (16 hr.; solvent front moved 37 cm.). 4-Hydroxypipecolic acid (R_F 0·20) was absent and the chromatogram showed pipecolic acid (R_F 0·36) and components with R_F 0·52 and 0·58, apparently 4-iodopipecolic acids, which gave purple colours with ninhydrin and a blue-green and a faint pink colour respectively with isatin; the iodo-acids gave brown colours with cold neutral silver nitrate solution. In a second experiment the reduction mixture (from 0·02 g. of acid) was treated with an excess of freshly prepared silver carbonate and solids were removed by centrifugation. The aqueous phase was chromatographed (15 hr.; solvent front moved 39 cm.) and showed none of the component of R_F 0·52, a trace of the component of R_F 0·58, and two new components, 2-aminopent-4-enoic acid (R_F 0·37) and baikiain (R_F 0·31). The former acid gave a purple colour with ninhydrin at 110—115° (but yellow green [25] at 80—90°) and a purple colour fading to pink with isatin, and baikiain gave a grey-green colour with ninhydrin and pink with isatin. Pipecolic acid was obscured by the aminopentenoic acid. The identity of the two components (R_F 0·31 and 0·37) was confirmed by their being inseparable on paper chromatograms (44 hr.) from baikiain (29·4 cm.) and authentic 2-aminopent-4-enoic acid (33·8 cm. from origin); pipecolic acid moved 34·2 cm. The same solutions were chromatographed with butan-1-ol–benzyl alcohol (1 : 1) on paper buffered with M/15-phosphate buffer [26] (pH 7·5) for 40 hr. and the amino-acids were detected with ninhydrin and isatin sprays containing much acetic acid, followed by heating at 110°. The acids gave the following distinctive colours (distances from origin in brackets): pipecolic acid (13 cm.) bright blue-violet with ninhydrin, green with isatin; baikiain (10·7 cm.) bright yellow with ninhydrin, brick red with isatin; 2-aminopent-4-enoic acid (7·7 cm.) brown with ninhydrin, white with isatin; proline (6·0 cm.) orange with ninhydrin, blue with isatin; 4-hydroxypipecolic acid (3·7 cm.) grey-brown with ninhydrin, green with isatin; and 5-hydroxypipecolic acid (3·5 cm.) yellow (with grey edges) with ninhydrin, green with isatin.

(c) *Formation of "norvaline" by hydrogenation of the reduction products.* 4-Hydroxypipecolic acid (0·02 g.) was heated with red phosphorus (0·0035 g.) and hydriodic acid (*d* 1·94; 0·2 c.c.) at 145° for 9 hr., the solution was then evaporated on a steam-bath, and the residue was dried in a desiccator over sodium hydroxide. A solution of the residue in water (1 c.c.) was treated with freshly prepared silver carbonate until no further reaction occurred, and the insoluble silver salts were separated at the centrifuge. Half the supernatant solution was hydrogenated over Adams catalyst at room temperature and pressure for 3 hr. Chromatograms of the hydrogenated solution showed 2-aminopentanoic acid (norvaline), R_F 0·49 (purple with ninhydrin, not fluorescing in ultraviolet light; pink with isatin); pipecolic acid, R_F 0·33 (blue-purple with ninhydrin, bright red fluorescence under ultraviolet light; green with isatin);

[25] Schlögl and Fabitschowitz, *Monatsh.*, 1954, **85**, 1060.
[26] McFarren, *Analyt. Chem.*, 1951, **23**, 168; Burroughs, *J. Sci. Food Agric.*, 1957, **8**, 122.

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4-hydroxypipecolic acid, R_F 0·16; and a minor component, R_F 0·10 (purple with ninhydrin, no fluorescence under ultraviolet light; pink with isatin). 4-Hydroxypipecolic acid (R_F 0·16), pipecolic acid (R_F 0·33), and baikiain (R_F 0·28) were used as standards on the same chromatogram. The norvaline spot at R_F 0·49 was very strong, and the colour reactions indicated the α-amino-acid structure; on paper chromatograms (15 hr.) it had R_F 0·49 and was distinguished from α-aminobutyric acid (R_F 0·28), leucine (R_F 0·54), and isoleucine (R_F 0·54). A mixture of the degradation product and authentic 2-aminopentanoic acid moved as a single component (R_F 0·45) on chromatograms run for 20 hr., but a mixture with valine was separated into 2-aminopentanoic acid (R_F 0·45) and valine (R_F 0·39). A mixture of valine (6·7 to 10·1 cm.) and norvaline (6·0 to 9·2 cm. from the origin) was incompletely separated when run on paper buffered with 0·067M-phosphate buffer at pH 7·5 developed with butan-1-ol–benzyl alcohol (1 : 1) for 30 hr.

Decarboxylation of 4*-Hydroxpipecolic Acid.*—Powdered 4-hydroxypipecolic acid (2 g.) in freshly distilled acetophenone (8 c.c.) was stirred and heated at 150° (bath) under nitrogen for 1½ hr. There was no apparent reaction and the temperature was raised to 190° for 1½ hr. The cooled mixture was diluted with ether (50 c.c.) and extracted with 2N-hydrochloric acid (10 c.c. and 2 × 5 c.c.). The acid extracts were washed with ether (20 c.c.), then evaporated under reduced pressure to a viscous residue (2·5 g.), to which were added water (2 c.c.) and potassium hydroxide (2 g.). Extraction with ether, evaporation, and distillation of the residue gave a colourless oil (0·52 g., 37%), b. p. *ca.* 219° (bath)/772 mm., which crystallised almost completely. The 4-hydroxypiperidine melted at 55—65° (capillary) and under the Leitz hot-stage microscope was seen to suffer a phase change at 57—60° to needles, m. p. 85—87°. Synthetic[27] 4-hydroxypiperidine similarly suffered a phase change at 59—60° and then melted at 85° alone or mixed with that obtained by decarboxylation of the imino-acid. The infrared spectra (2—11·5 μ; in $CHCl_3$) of the two samples were identical. The dimorphic 1-toluene-*p*-sulphonyl derivative crystallised from aqueous ethanol in needles, m. p. 114—115°, not depressed by admixture with synthetic 4-hydroxy-1-toluene-*p*-sulphonylpiperidine, m. p. 115—116°. The latter sometimes resolidified and melted again at 125°, and sometimes crystallised from aqueous ethanol in needles, m. p. 123—124° after sintering at 115° (capillary). Under the hot-stage microscope the substance had m. p. 125—126° with change of crystalline form at 117° (lit.,[28] m. p. 131—132°, from benzene).

Oxidation of 4*-Hydroxy- to* 4*-Oxo-*L*-pipecolic Acid* (V).—The following procedure was adopted after numerous trials to determine the optimum conditions for oxidation and isolation: 8N-Chromic acid in aqueous sulphuric acid[29] (7·5 c.c.) was added to 4-hydroxypipecolic acid (2·18 g., containing *ca.* 3% of pipecolic acid) in acetic acid (150 c.c.; purified over chromic acid), concentrated sulphuric acid (1·73 c.c.), and water (5 c.c.), and the temperature was kept below 20° by intermittent cooling. After 1½ hr. methanol (5 c.c.) was added and next day the solution was decanted from chromium salts. The combined solutions from four such oxidations were evaporated under reduced pressure to *ca.* 40 c.c. and, after dilution with water, sulphate was removed with barium carbonate, and excess of barium was removed with sulphuric acid. The solution was added to a ZeoKarb 225 column (200 g.; 2·5 × 53 cm.) (H^+ form) and eluted in the following fractions: 1, feed solution; 2, water (250 c.c.); 3—10, 0·1N-HCl (2 l.); 11—12, 0·2N-HCl (500 c.c.); 13—16, 0·4N-HCl (1 l.); 17—20, 0·8N-HCl (1 l.); 21—22, water (500 c.c.); 23—27, 3N-ammonia (1 l.). Fractions were evaporated on a steam-bath, and the residues were examined by paper chromatography (12 hr.; solvent front moved 27·4 cm.). Chromium was present in fractions 1—6 and 17—20; the keto-acid was present in fractions 11—16 and gave an elongated spot R_F 0·20; β-alanine (R_F 0·24) in fractions 16—20; and pipecolic acid (R_F 0·35) in fractions 19—20. The first ammoniacal eluate (fraction 24) contained some of each amino-acid, especially pipecolic acid. The mixtures of amino-acids in some of the fractions were separated on a 50 g. column of ZeoKarb 225. The keto-acid fractions were combined and evaporated to a thin syrup which on cooling gave *4-oxo-*L*-pipecolic acid hydrochloride monohydrate* (1·28 g.) in needles, decomp. 203°, $[\alpha]_D^{21}$ +3·8° (2% in H_2O) (Found, on an air-dried sample: loss at 80°, 8. $C_6H_9O_3N,HCl,H_2O$ requires H_2O, 9·1. Found, on a sample dried for 6 hr. *in vacuo*: C, 39·9; H, 5·65; N, 7·3; Cl, 19·4. $C_6H_9O_3N,HCl$ requires C, 40·1; H, 5·6; N, 7·8; Cl, 19·7%). Crystallisation after dilution of the mother-liquors with propan-2-ol gave a

[27] Bowden and Green, *J.*, 1952, 1164.
[28] Arndt and Kalischek, *Ber.*, 1930, **63**, 587.
[29] Djerassi, Engle, and Bowers, *J. Org. Chem.*, 1956, **21**, 1547 (footnote 10).

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further 2·35 g. in needles, and further manipulation gave more keto-acid (total 4·3 g., 36%) which includes 4% recovered from the chromium salts. The free acid was obtained from the hydrochloride (0·4 g.) by elution from a ZeoKarb 225 column (28 g.) with N-ammonia. Evaporation under reduced pressure and dilution with propan-2-ol gave (−)-*4-oxo-L-pipecolic acid monohydrate* as prisms (0·19 g.), decomp. 240°, $[\alpha]_D^{23}$ −14·8° (1% in H_2O) (Found: C, 44·3; H, 7·0; N, 8·5. $C_6H_9O_3N,H_2O$ requires C, 44·7; H, 6·9; N, 8·7%).

β-Alanine fractions were collected and evaporation left a crystalline residue (0·59 g.) containing pipecolic acid which was converted by phenyl isocyanate into the phenylcarbamoyl derivatives (0·27 g.), m. p. 146—157°, from which pipecolic acid phenylhydantoin and *N*-phenylcarbamoyl-β-alanine (0·17 g., 1·5% from 4-hydroxypipecolic acid), m. p. 164—169°, were separated by dissolution in aqueous sodium carbonate. Authentic *N*-phenylcarbamoyl-β-alanine crystallised from water in blades, m. p. 173—174° (lit.,[30] m. p. 171°), mixed m. p. with the oxidation product 170—172°. Further *N*-phenylcarbamoyl-β-alanine (0·11 g., total 0·28 g., 2·2%) was recovered from the chromium salts.

4′-Oxo-3-phenylpiperidino(1′,2′:1,5)hydantoin.—Phenyl isocyanate (0·30 g., 1·25 equiv.) was added with shaking during 15 min. to an ice-cooled solution of 4-oxo-L-pipecolic acid hydrochloride (0·4 g.) in 0·5N-sodium hydroxide (8 c.c.). The filtrate from diphenylurea was acidified and next day the (−)-*hydantoin* was collected as needles, m. p. 187°, insoluble in aqueous sodium carbonate (Found: C, 63·8; H, 5·05; N, 11·3. $C_{13}H_{12}O_3N_2$ requires C, 63·9; H, 4·95; N, 11·5%). A solution in ethanol (0·1 g. in 25 c.c.), prepared by warming, showed mutarotation from −0·94° to −0·437° after 23 hr. The solution was boiled for 6 hr. and then concentrated to *ca.* 1 c.c. before slow crystallisation gave the recovered hydantoin (0·05 g.), m. p. and mixed m. p. 187°. The recovered material had $[\alpha]_D^{23}$ −55° (0·16% in EtOH, dissolved with heating). Recrystallisation of the phenylhydantoin (0·15 g.) from ethanol (10 c.c.) as rapidly as possible gave needles (0·102 g.), m. p. 187°. A solution in ethanol prepared in the cold exhibited $[\alpha]_D^{23}$ −87° (0·366% in EtOH) 10 min. after preparation.

(−)-cis-*4-Hydroxy-L-pipecolic Acid* (VI).—A solution of 4-oxo-L-pipecolic acid hydrochloride monohydrate (2 g.) in water (20 c.c.) was adjusted to pH 9·0 with N-potassium hydroxide (16·6 c.c.) and cooled to 20° while an aqueous solution of sodium borohydride (0·112 g., 1·2 equiv.) was added in portions. The temperature of the solution rose after each adition, and the solution was kept at room temperature for 1 hr. and then just acidified with acetic acid. The solution was added to a ZeoKarb 225 column (28 g., 1·2 × 27 cm.) (H^+ form), and the amino-acids were recovered with N-ammonia. Evaporation gave a thin syrup which crystallised [1·05 g.; m. p. 265° (decomp.)] after addition of ethanol. A second crop (0·23 g.) had m. p. 250—263° (decomp.) and left 0·27 g. in the mother-liquors. Paper chromatography (40 hr.) showed that the crystalline fractions contained mainly *cis*-acid with a trace of the natural isomer, and the latter predominated in the mother-liquor. (−)-cis-*4-Hydroxy-L-pipecolic acid monohydrate* (78%) crystallised from aqueous ethanol in plates, m. p. 265° (decomp.), $[\alpha]_D^{23}$ −17° (1·1% in H_2O), $[\alpha]_D$ +7° (1·1% in 5N-HCl) (Found: C, 43·6; H, 8·1; N, 8·5; loss on drying at 80° *in vacuo*, 11·6. $C_6H_{11}O_3N,H_2O$ requires C, 44·2; H, 8·0; N, 8·6; H_2O, 11·0%). The acid sometimes crystallised from aqueous ethanol as a *dihydrate*, m. p. 265° (decomp.) (Found: C, 39·7; H, 8·2; N, 7·7; loss on drying at 80° *in vacuo*, 19·0. $C_6H_{11}O_3N,2H_2O$ requires C, 39·8; H, 8·3; N, 7·7; loss, 19·9%). The *copper salt* crystallised from water in deep blue plates, m. p. 245° (decomp.), which did not lose weight over anhydrous calcium chloride (Found: N, 6·6; CuO, 16·9. $C_{21}H_{20}O_6N_2Cu,4H_2O$ requires N, 6·6; CuO, 18·7%). The N-(*2,4-dinitrophenyl*) *derivative* (62%) crystallised from aqueous ethanol in yellow prisms, m. p. 134° (Found: C, 45·0; H, 4·2; N, 13·1. $C_{12}H_{13}O_7N_3,\frac{1}{2}H_2O$ requires C, 45·0; H, 4·4; N, 13·1%).

(−)-cis-1-*Benzoyl-4-hydroxy-L-pipecolic Acid.*—Benzoyl chloride (0·15 g., 1·1 equiv.) was added in portions to the *cis*-acid monohydrate (0·163 g.) in ice-cooled 0·7N-sodium hydroxide (3·2 c.c.), with shaking, the filtrate was acidified, and light petroleum added to dissolve benzoic acid. After 14 hr. at 0° the N-*benzoyl derivative* crystallised from the aqueous layer in blades (0·119 g.), m. p. 104°, $[\alpha]_D^{23}$ −39·5° (1% in EtOH) (Found: C, 58·5; H, 6·5; N, 5·2. $C_{13}H_{15}O_4N,H_2O$ requires C, 58·4; H, 6·4; N, 5·2%). The same product was obtained when 2·2 equiv. of benzoyl chloride were used. The ethanolic solution (1%; 10 c.c.) used in the polarimeter was evaporated after addition of water, and the derivative crystallised slowly at 0° in a *form* (blades) (0·076 g., 76% recovery), m. p. 191°, $[\alpha]_D^{26}$ −38·5° (1% in EtOH) (Found: C, 58·7; H, 6·4; N, 5·2%). It is thus dimorphic and a mixture of the first form (m. p. 104°) with

[30] Fischer and Leuchs, *Ber.*, 1902, **35**, 3787.

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the second (m. p. 191°) melted at 191°. Both forms dissolved readily in aqueous sodium hydrogen carbonate and gave similar infrared spectra (in $CHCl_3$; calcium fluoride prism) in the recorded range 2—6·5 μ.

4-Benzyloxypicolinic Acid.—Methyl 4-chloropicolinate (37%), m. p. 48—52°, was prepared according to Mosher and Look,[31] who report m. p. 57—58° and 71% yield. Sodium (1 g.) was dissolved in benzyl alcohol (30 c.c.) almost at the b. p. (to reduce its viscosity) and the cold solution was added in portions, with stirring, to a solution of methyl 4-chloropicolinate (3·43 g.) in benzyl alcohol. The mixture was boiled gently for 45 min. and was then cooled (it became gelatinous), and water (50 c.c.), ether (100 c.c.), and 2N-hydrochloric acid (50 c.c.) were added. The mixture was shaken and the ether layer was washed twice with 2N-hydrochloric acid and discarded. The acidic extracts were combined and washed with ether, and 5N-sodium hydroxide (50 c.c.) was added. This caused separation of crystals and the mixture was boiled to remove dissolved ether and then stored at 0°. Next day the crystalline sodium 4-benzyloxypicolinate (3·65 g.) was collected and dissolved in hot water (20 c.c.), and acetic acid (1·3 c.c., a slight excess) was added. The acid (2·95 g.) crystallised at 0° during 2 days and recrystallisation from ethanol (charcoal) gave *4-benzyloxypicolinic acid* (2·4 g., 52%) in prisms, m. p. 172° (Found: C, 68·4; H, 5·0; N, 5·9. $C_{13}H_{11}O_3N$ requires C, 69·1; H, 4·8; N, 6·1%). The *hydrochloride monohydrate* (83%) crystallised in needles, m. p. 158° raised to 162° by recrystallisation from 5N-hydrochloric acid (Found: C, 55·2; H, 5·0; N, 4·6; Cl, 13·2. $C_{13}H_{12}O_3N,HCl,H_2O$ requires C, 55·0; H, 5·0; N, 4·9; Cl, 13·5%). When heated above its m. p. crystals appeared in the melt (at *ca.* 205°) and melted again at 238—250° (decomp.). The hydrochloride (0·39 g.) was heated at 200°, whereupon it melted and resolidified, and gave a liquid distillate with the odour of benzyl chloride. The solid product was washed with light petroleum (b. p. 60—80°) before crystallisation from water gave 4-hydroxypicolinic acid (0·15 g., 73%) in prisms, m. p. 258° (decomp.) alone or mixed with that obtained by hydrogenolysis of 4-benzyloxypicolinic acid.

Hydrogenation of 4-Benzyloxypicolinic Acid.—Hydrogenation of 4-benzyloxypicolinic acid (1 g.) in 5N-hydrochloric acid (20 c.c.) at room temperature and pressure over Adams catalyst (0·1 g.) proceeded rapidly with complete dissolution of the compound in 2 hr. Hydrogen uptake ceased after 29 hr. and the solution contained pipecolic acid as the only ninhydrin-positive or isatin-positive material. The filtered and concentrated solution deposited 4-hydroxypicolinic acid (0·52 g., 85%) in prisms of m. p. varying between 255° and 258° (Found: C, 51·7; H, 3·6; N, 10·1. Calc. for $C_6H_5O_3N$: C, 51·8; H, 3·6; N, 10·1%). Hydrogenation was inhibited in 1·5N-ammonia but in acetic acid at 65° (and at 105°) hydrogenation gave pipecolic acid and *cis*-4-hydroxypipecolic acid detectable by paper chromatography, and better results were obtained by hydrogenation in water.

4-Benzyloxypicolinic acid (6·46 g.) in water (50 c.c.) was hydrogenated at 105°/70 atm. over Adams catalyst (0·285 g.) for 24 hr. and then filtered. The pale filtrate darkened rapidly and after concentration was again filtered from much dark brown material. The 4-hydroxypipecolic acids were isolated from the soluble mixture (1·91 g.) by preparative paper chromatography on Whatman seed-test paper [32] with the upper phase of the system ethyl acetate–ethanol–acetic acid–water (6 : 1 : 2 : 1). The imino-acid mixture in water (12 c.c.) was placed in a strip (total width 150 cm.), and the upper phase from 300 c.c. of the solvent mixture was used for each 15 cm. Chromatography gave after *ca.* 24 hr. bands of pipecolic acid at 40—48 cm. and the 4-hydroxypipecolic acids at 22—34 cm. Bands were located by heating the paper after spraying it lightly with ninhydrin, and the 4-hydroxypipecolic acids (0·32 g., 8%) were extracted from the appropriate areas with 90% ethanol (Soxhlet), but failed to crystallise. The crude acids were transferred to a ZeoKarb 225 column and elution with 0·1, 0·2, 0·4, and 0·8N-hydrochloric acid (250 c.c. each) gave the 4-hydroxypipecolic acids completely in the last two solvents. A solution of the product (0·29 g.) in dilute hydrochloric acid (charcoal) was concentrated and deposited the (±)-*cis*-4-hydroxypipecolic acid hydrochloride (0·075 g., 1·4%) in prisms, m. p. 253—255° (decomp.), and shown by paper chromatography to contain the *cis*-acid as the only ninhydrin-positive component.

Epimerisation of 4-Hydroxypipecolic Acid and Comparisons with Other Hydroxypipecolic Acids.—(*a*) The *trans*-acid (6 mg.) gave a mixture of *cis*- and *trans*-isomers when heated with N-sodium hydroxide (0·1 c.c.) in a sealed tube at 145° for 9 hr. A trace of the epimer was similarly produced by heating in water alone, but not in N-hydrochloric acid.

[31] Mosher and Look, *J. Org. Chem.*, 1955, **20**, 283.
[32] Brownell, Hamilton, and Casselman, *Analyt. Chem.*, 1957, **29**, 550.

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(*b*) The epimeric mixture of imino-acids formed by heating *trans*-4-hydroxypipecolic acid (5 mg.) in saturated aqueous barium hydroxide (0·3 c.c.) in a sealed tube at 155° for 12 hr. was compared with 5-hydroxypipecolic acid obtained from dates,[6] (−)-*cis*-4-hydroxypipecolic acid (provided by Dr. Vanderhaeghe), (±)-*cis*-3-hydroxypipecolic acid,[8] and with Fowden's acid.[2] On paper chromatograms run for 28, 48, and 84 hr. the acids moved as follows: 4-hydroxypipecolic acid from *Acacia* sp. 12·0, 19·1, and 35·5 cm.; 5-hydroxypipecolic acid the same in each case; *cis*-acid from epimerisation 8·7, 16·6, and 31·3 cm., and pipecolic acid 20·8, 32·2 cm. and off the paper. 5-Hydroxypipecolic acid gave a blue-purple colour (and a bright red fluoresence under ultraviolet light) when heated with ninhydrin, and was thus easily distinguished from the natural 4-hydroxy-acid. In phenol–water and an atmosphere containing ammonia and hydrogen cyanide,[33] for 12 and 24 hr. (solvent front moved 27 and 45 cm.), the 4-hydroxy-epimers were not separated and had R_F 0·55 and 0·47; 5-hydroxypipecolic acid R_F 0·53 and 0·45; pipecolic acid R_F 0·33 and 0·27. The synthetic 4-hydroxy-acid was similarly epimerised to a mixture of *cis*- and *trans*-forms indistinguishable from the mixture derived from the natural acid. *cis*-3-Hydroxypipecolic acid (R_F 0·24) was clearly separated from the natural acid and its epimer, and after being heated with barium hydroxide showed several ninhydrin-positive materials all distinguishable from the natural 4-hydroxy-acid and its epimer.

(*c*) (−)-*trans*-*N*-Benzoyl-4-hydroxypipecolic acid (2·49 g.) was heated at 200° for 5 min., then boiled with 6N-hydrochloric acid (100 c.c.) for 6½ hr., and benzoic acid was removed with light petroleum. The aqueous layer was shown by paper chromatography to contain *cis*- and *trans*-4-hydroxypipecolic acid, which after passage through a ZeoKarb 225 column were converted into the copper salts. Crystallisation of these salts gave fractions each shown to contain *cis*- and *trans*-acid in approximately equal quantities (Found, on the first fraction: N, 6·7; CuO, 17·0. Calc. for $C_{12}H_{20}O_6N_2Cu,4H_2O$: N, 6·6; CuO, 18·7%).

(+)-1-*Acetyl*-4-*hydroxy*-D-*pipecolic Lactone* (VII) *and* (+)-cis-4-*Hydroxy*-D-*pipecolic Acid* (VIII).—(−)-*trans*-4-Hydroxy-L-pipecolic acid (2·9 g.) was boiled with acetic acid (30 c.c.) and acetic anhydride (10·2 c.c., 5 equiv.) for 4 hr. The solution was evaporated under reduced pressure, and the brown crystalline residue was dissolved in ethyl acetate (60 c.c.) and decolorised with charcoal before concentration (to 15 g.). Crystallisation at 0° for 18 hr. gave (+)-1-*acetyl*-4-*hydroxy*-D-*pipecolic lactone* in thick, pale brown plates (1·1 g., 32%), m. p. 145° raised to 148—149° by recrystallisation (charcoal) from ethyl acetate, $[\alpha]_D^{24}$ +181° (1% in EtOH), +190° (1% in $CHCl_3$) (Found: C, 57·2; H, 6·6; N, 8·3. $C_8H_{11}O_3N$ requires C, 56·8; H, 6·55; N, 8·3%).

The lactone (1·0 g.) was boiled with 2N-hydrochloric acid (50 c.c.) for 3 hr. before evaporation on a steam-bath. The crystalline residue was dissolved in water (charcoal) and transferred to a ZeoKarb 225 column (28 g.) and the imino-acid was eluted with N-ammonia. Concentration gave a syrup which crystallised, after the addition of ethanol, in prisms (0·74 g., 68%), m. p. 266—269° (decomp.), consisting of (+)-cis-4-*hydroxy*-D-*pipecolic acid dihydrate*, $[\alpha]_D^{24}$ +17° (1% in H_2O), −6·1° (1% in 5N-HCl) (Found: C, 39·8; H, 8·3; N, 8·1; loss on drying at 80° *in vacuo*, 19·3. $C_6H_{11}O_3N,2H_2O$ requires C, 39·8; H, 8·3; N, 7·7; H_2O, 19·9%). The acid was chromatographically indistinguishable from Dr. Vanderhaeghe's (−)-*cis*-acid and from the epimer of the natural *trans*-acid.

L-*Pipecolic Acid and Derivatives*.—L-Pipecolic acid was obtained from *A. excelsa* heartwood in prisms, m. p. 273—275° (decomp.) (lit.,[34] m. p. 274°), $[\alpha]_D^{23}$ −25·2° (2·2% in H_2O) (lit.,[35] −25·2°) (Found: C, 56·2; H, 8·6; N, 11·0. Calc. for $C_6H_{11}O_2N$: C, 55·8; H, 8·6; N, 10·9%). The (−)-hydrochloride, $[\alpha]_D^{22}$ −10·5° (6% in H_2O) (lit.,[35] −5° to −10·3°), $[\alpha]_D^{23}$ −10·5° (2% in 5N-HCl), −10·0° (6% in 5N-HCl), had m. p. 256—258° (decomp.) (lit.,[14] 256° and [36] 258—259°) alone and when mixed with the (±)-hydrochloride. *N*-Benzoyl-L-pipecolic acid crystallised from ethanol–light petroleum, b. p. 60—80°, in prisms, m. p. 133° depressed to 119—122° on admixture with the (±)-benzoyl derivative, and crystallisation from water gave needles, m. p. 132—133°, $[\alpha]_D^{22}$ −72° (1% in EtOH) (lit.,[14] m. p. 145°, $[\alpha]_D$ −72·8°). 1-*Phenylcarbamoyl*-L-*pipecolic acid* (80%) crystallised in prisms, m. p. 178°, from an acidified solution in 5% aqueous sodium carbonate, and had $[\alpha]_D^{20}$ −39° (1% in EtOH) (Found: C, 63·4; H, 6·4; N, 11·4. $C_{13}H_{16}O_3N_2$ requires C, 62·9; H, 6·5; N, 11·3%). Recrystallisation from boiling water gave the optically inactive phenylhydantoin in needles, m. p. 159—160°.

[33] Consden, Gordon, and Martin, *Biochem. J.*, 1944, **38**, 224.
[34] Grobbelaar, Zacharius, and Steward, *J. Amer. Chem. Soc.*, 1954, **76**, 2912.
[35] Harris and Pollock, *Chem. and Ind.*, 1953, 462.
[36] Zacharius, Thompson, and Steward, *J. Amer. Chem. Soc.*, 1954, **76**, 2908.

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1-*Phenylcarbamoyl*-DL-*pipecolic Acid and* 3-*Phenylpiperidino*-(1′,2′:1,5)*hydantoin.*—(±)-Pipecolic acid hydrochloride, m. p. 258—260° (decomp.), was obtained (91%) by hydrogenation of picolinic acid (5 g.) in 5N-hydrochloric acid (20 c.c.) over Adams catalyst (0·2 g.) at 25 atm./60° for 24 hr. This salt (0·66 g.) in N-sodium hydroxide (8 c.c.) was treated with phenyl isocyanate (0·59 g., 1·25 equiv.). Acidification of the filtrate gave crystals of the (±)-1-*phenylcarbamoylpipecolic acid* (0·81 g., 81%), m. p. 138° and 156—158° after resolidification (cyclisation) (Found: C, 63·4; H, 6·8; N, 11·4. $C_{13}H_{16}O_3N_2$ requires C, 62·9; H, 6·5; N, 11·3%). Recrystallisation from hot water, after boiling for 1 hr., gave the (±)-*hydantoin* in needles, m. p. 158—159° alone and when mixed with that formed by cyclisation of the (−)-phenylcarbamoyl derivative (Found: C, 67·8; H, 6·2; N, 12·2. $C_{13}H_{14}O_2N_2$ requires C, 67·8; H, 6·1; N, 12·2%).

Ethyl 1-*Ethoxycarbonyl*-3-*oxopyrrolidin*-2-*ylacetate* (X).—Ethyl β-ethoxycarbonylaminopropionate [37] (38·1 g., 0·2 mole) and ethyl fumarate [38] (34·4 g., 0·2 mole) were added successively to a stirred mixture of dry benzene (350 c.c.) and sodium wire (4·6 g., 0·2 g.-atom). Reaction began slowly and the temperature rose to the b. p. during 45 min. and stirring was then discontinued for 30 min. while the last pieces of sodium reacted; and the reddish-brown solution was then boiled and stirred for 30 min. The cooled solution was diluted with ether (100 c.c.) and shaken with ice-water (300 c.c.), and the almost colourless organic phase was extracted with ice-water (2 × 75 c.c.). The combined aqueous phases were extracted with ether (75 c.c.) before being poured into ice (75 g.) and concentrated sulphuric acid (6·5 c.c.), whereupon an oil separated. The strongly acidic solution was saturated with sodium chloride before being extracted with ethyl acetate (3 × 100 c.c.), and the extracts were washed with brine (50 c.c.) containing sodium hydrogen carbonate, and dried (Na_2SO_4). Removal of the ethyl acetate and distillation under reduced pressure gave an oil (53·5 g.) which was dissolved in 10N-hydrochloric acid (150 c.c.). Next day the solution was evaporated under reduced pressure; ethanol (2 × 100 c.c.) was added to the residue, and the mixture evaporated to dryness. The residue was boiled for 4½ hr. with ethanol (150 c.c.) previously saturated with hydrogen chloride, and the solution was then evaporated under reduced pressure; distillation of the residue (37 g.) gave *ethyl* 1-*ethoxycarbonyl*-3-*oxopyrrolidin*-2-*ylacetate* (24·2 g., 50%), b. p. 122—128° (mainly at 125°)/0·3 mm. (Found: C, 53·9; H, 7·0; N, 6·0. $C_{11}H_{17}O_5N$ requires C, 54·3; H, 7·0; N, 5·8%), and a fraction (2·9 g.), b. p. 128—136°/0·3 mm., which yielded the same semicarbazone as the main fraction. Infrared absorption (in Nujol or CCl_4) included carbonyl bands at 5·68, 5·77, and 5·86 μ. The *semicarbazone* prepared at room temperature (7 days) crystallised from ethanol in prisms, m. p. 124° (Found: N, 18·9. $C_{12}H_{20}O_5N_4$ requires N, 18·7%). The dimorphic 2,4-*dinitrophenylhydrazone*, orange plates, m. p. 112—113°, or yellow prisms, m. p. 135°, was obtained in either form by appropriate seeding of a supersaturated ethanolic solution. The lower-melting form sometimes resolidified and then melted again at 133—135° (Found, for the orange form: N, 16·6; for the yellow form: N, 16·4. $C_{17}H_{21}O_8N_5$ requires N, 16·5%).

3-*Hydroxypyrrolidin*-2-*ylacetic Acid* (XI).—Sodium borohydride (0·38 g., 2 equiv.) in water (1 c.c.) was added dropwise during 10 min. to a solution of the above keto-ester (4·86 g.) in ethanol (50 c.c.) initially at 15° and kept below 20° by cooling. After 40 min. 10% sulphuric acid was added until all the borohydride was decomposed. Barium hydroxide octahydrate (19 g.) and water (50 c.c.) were added and the mixture was heated in a boiling-water bath for 16 hr. The mixture was diluted with water (100 c.c.) and filtered when cold. The solution was acidified with 10% sulphuric acid, and the filtrate was continuously extracted with ether for 16 hr. to remove boric acid (0·073 g.). The aqueous solution was basified with aqueous barium hydroxide, and the filtered solution was extracted with ether for 30 hr. before removal of barium as carbonate. Evaporation of the filtrate left a crystalline residue which was digested with ethanol containing a few drops of acetic acid, and the insoluble material (1·11 g., 38%; m. p. 192—198°) was collected; the filtrate contained at least seven ninhydrin-positive substances, and was discarded. The solid appeared to be a single substance and chromatography (19 hr.; solvent front moved 48 cm.) showed a substance with R_F 0·27 (4-hydroxypipecolic acid, R_F 0·20; pipecolic acid, R_F 0·36) which gave a yellow-orange colour with ninhydrin and a white spot with isatin detectable as a non-absorbing area under ultraviolet light. Three crystallisations from aqueous ethanol (charcoal) gave 3-*hydroxypyrrolidin*-2-*ylacetic acid monohydrate* (0·51 g.) in prisms, m. p. 215—216° (decomp.) (Found, on material dried *in vacuo* for 24 hr.: C, 44·5; H,

[37] Braun and Looker, *J. Amer. Chem. Soc.*, 1958, **80**, 359.
[38] Mitchovitch, *Bull. Soc. chim. France*, 1937, **4**, 1661; *Chem. Abs.*, 1938, **32**, 1241.

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8·0; N, 8·6. $C_6H_{11}O_3N,H_2O$ requires C, 44·2; H, 8·0; N, 8·6%). The N-(2,4-*dinitrophenyl*) *derivative* (83%) crystallised from aqueous ethanol in prisms, m. p. 205° (Found: C, 45·2; H, 4·6; N, 12·9. $C_{12}H_{13}O_7N_3,\frac{1}{2}H_2O$ requires C, 45·0; H, 4·4; N, 13·1%). The imino-acid was recovered after treatment with nitrous acid under conditions which destroyed added glycine and β-alanine. The phenylcarbamoyl derivative formed from the acid and phenyl isocyanate lost the elements of water to give the *lactone*, which crystallised from water in prisms, m. p. 168°, insoluble in cold aqueous sodium hydrogen carbonate (Found: C, 63·3; H, 5·6; N, 11·4. $C_{13}H_{14}O_3N_2$ requires C, 63·4; H, 5·7; N, 11·4%). The lactone was recovered after being heated with 3N-hydrochloric acid on a steam-bath for 8 hr. In Nujol mull it showed NH absorption at 2·95 μ and carbonyl bands at 5·69 (lactone) and 6 μ (urea).

The authors thank Mr. A. G. Moritz for infrared measurements, Dr. L. Fowden for a specimen of 4-hydroxypipecolic acid from *Armeria maritima*, Dr. H. Vanderhaeghe for (−)-*cis*-4-hydroxypipecolic acid, Dr. H. Plieninger for 3-hydroxypipecolic acid, and Dr. T. J. King for baikiain. This investigation was prosecuted during tenure of a General Motors Holden Fellowship (by P. I. M.).

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36. *Reduced Cyclic Compounds. Part X.* The Synthesis of 1-1′-Acetoxyvinyl-3,4-dihydronaphthalene and its Reactions with Some Dienophils.*

By M. F. ANSELL and G. T. BROOKS.

The preparation of 1-1′-acetoxyvinyl-3,4-dihydronaphthalene and its reactions with maleic anhydride, benzoquinone, and 2,6-xyloquinone are described.

THE preparation of 1-1′-acetoxyvinylcyclohexene and its reactions with dienophils have been described.[1] We now report a similar study with 1-1′-acetoxyvinyl-3,4-dihydronaphthalene which was prepared by the reaction sequence (I) ⟶ (V). The reduction[2] of 1-naphthoic acid (I) to 1,4-dihydronaphthoic acid (II) by addition of sodium to a solution of the acid and sodamide in liquid ammonia could not be repeated, and reduction was conveniently effected by addition of sodium to a solution of the acid in liquid ammonia containing ethanol (cf. the reduction of *o*-toluic acid[3]). There is little agreement (see Experimental section) among the recorded melting points of 1,4-dihydronaphthoic acid (II) and it is possible that the reduction product may contain some of the 3,4-dihydro-acid (III). Various procedures have been described[4] for the conversion of the 1,4- into the 3,4-dihydro-acid (III). It was found that use of boiling 10% potassium hydroxide solution gave an acid whose melting point (119—120° on small scale, 115—119° on 0·3-molar scale) was close to the most reliable recorded value[5] (121°). The 3,4-dihydro-acid was converted into the acid chloride by treatment with thionyl chloride. The melting point of the derived amide was considerably higher than that recorded by Birch and Robinson,[6] but agreed with that reported earlier by Ranedo.[7] The acid chloride was readily converted into 1-acetyl-3,4-dihydronaphthalene (IV), but methylcadmium was

* Part IX, *J.*, 1960, 5219.

[1] (a) Ansell and Brooks, *J.*, 1956, 4518; (b) Nazarov, Kucherov, Andreev, and Segal, *Doklady Akad. Nauk S.S.S.R.*, 1955, **104**, 729; (c) Winternitz and Balmossière, *Tetrahedron*, 1958, **2**, 100.

[2] Birch, *J.*, 1944, 430.

[3] Birch, *J.*, 1950, 1551.

[4] Elsevier's "Encyclopedia of Organic Chemistry," Amsterdam, 1953, **12**, *B*, p. 4069.

[5] Fieser and Holmes, *J. Amer. Chem. Soc.*, 1936, **58**, 2319.

[6] Birch and Robinson, *J.*, 1944, 503.

[7] Ranedo, *Anales real Soc. españ. Fís. Quím.*, 1927, **25**, 429.

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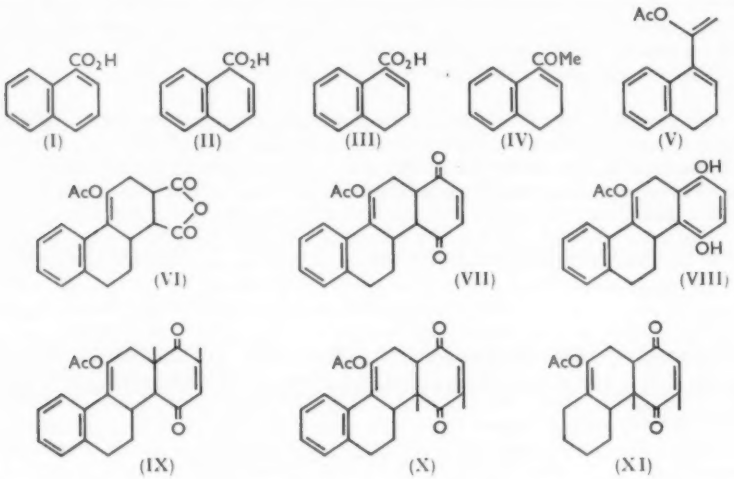
preferable to the dimethylzinc used by Birch and Robinson.[6] This ketone afforded a bright-red (characteristic of αβ-unsaturated ketones) 2,4-dinitrophenylhydrazone, different from that previously recorded [6] together with a small amount of an isomeric derivative. The latter was not identified, but may be a pyrazoline derivative.[8] The ultraviolet absorption spectrum of this ketone, which contains a cross-conjugated system, has a single



maximum at 278 mμ. It is reported [9] that various 2-phenylcyclohex-2-enones which contain a similar cross-conjugated system, show absorption at 268—270 mμ. The more rigid chromophoric system in the ketone (IV) may explain the bathochromic shift in the ultraviolet absorption maximum of this ketone as compared with that of the 2-phenylcyclohex-2-enones. Treatment of 1-acetyl-3,4-dihydronaphthalene with isopropenyl acetate in the presence of toluene-*p*-sulphonic acid gave the expected 1-1′-acetoxyvinyl-3,4-dihydronaphthalene (V).

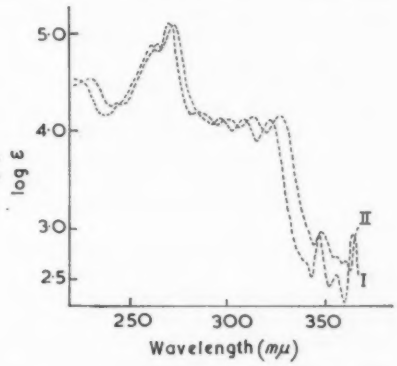
The diene (V) with maleic anhydride yielded 4-acetoxy-1,2,3,9,10,11-hexahydrophenanthrene-1,2-dicarboxylic anhydride (VI), which was hydrolysed by boiling water to the acid. The latter, as the dimethyl ester, formed a 2,4-dinitrophenylhydrazone, indicating the presence of a potential carbonyl group. The ultraviolet absorption spectrum of the free acid ($\lambda_{max.}$ 252 mμ in EtOH) resembles that recorded for β-methylstyrene [10] and 1-phenylcyclohexene [11] both of which contain a similar chromophore. Some similarity is also shown, with the expected hypsochromic shift due to the absence of the 7-methoxy-group, to the spectrum of 1,2,3,9,10,11-hexahydro-7-methoxyphenanthrene-1,2-dicarboxylic acid,[12] although the shoulder at long wavelength which has been used as a criterion of the presence of a 3,4-double bond is absent. There is no doubt, however, that the double bond is in this position, both from the conditions used to prepare the adduct and from the fact that the product forms a 2,4-dinitrophenylhydrazone.

With benzoquinone the diene (V) gave 11-acetoxy-1,4,5,6,10,13,14,15-octahydro-1,4-dioxochrysene (VII). The gross structure of this adduct was shown by its degradation to chrysene, and its detailed structure from its infrared absorption spectra which showed

[8] Cf. Nazarov and Gurvich, *J. Gen. Chem. U.S.S.R.*, 1955, **25**, 1677.
[9] Bornstein, Pappo, and Szmuszkovicz, *Bull. Res. Council Israel*, 1952, **2**, 273.
[10] Friedel and Orchin, " Ultra-violet Spectra of Aromatic Compounds," Chapman and Hall, London, 1951, spectrum no. 24.
[11] Carlin and Landerl, *J. Amer. Chem. Soc.*, 1953, **75**, 3969.
[12] Bachmann and Controulis, *J. Amer. Chem. Soc.*, 1951, **73**, 2636.

absorption at 5·7 μ, characteristic of the enol acetate group, together with the absence of absorption in the hydroxy-region [eliminating a structure such as (VIII)].

The Diels–Alder reaction of the diene (V) with 2,6-xyloquinone gave a single product, which existed in two polymorphic forms. This adduct may have either of the structures (IX) and (X), the latter being analogous to that (XI) of the adduct from 1-1′-acetoxyvinylcyclohexene and 2,6-xyloquinone. Degradation of the adduct (IX or X) by reduction with lithium aluminium hydride, followed by dehydration and dehydrogenation with selenium, did not give rise to either 2- or 3-methylchrysene (a synthesis of the latter is described), but to a substance whose ultraviolet spectrum shows a bathochromic shift of 4—5 mμ in the fine structure region as compared with 3-methylchrysene. Such a spectral shift is characteristic [13] of a dimethylchrysene (see Figure). The degradation product is not identical with any of the known dimethylchrysenes or with those subsequently synthesised.[14] These results although showing the tetracyclic skeleton of the



Absorption spectra of (I) *3-methylchrysene and* (II) *a degradation product* (? *a dimethylchrysene*) *in cyclohexane.*

Diels–Alder addition product from the diene (V) and 2,6-xyloquinone do not establish the position of the angular methyl group, which is tentatively assigned to the 14-position by analogy with the structure of the tricyclic adduct (XI).

Added in Proof.—Winternitz and Diaz (*Compt. rend.*, 1960, **250**, 3433; *Bull. Soc. chim. France*, 1959, 1444) have reported the preparation of 1-1′-acetoxyvinyl-3,4-dihydronaphthalene from 1-acetyl-3,4-dihydronaphthalene obtained by a different route from that used by us. The ultraviolet spectrum of the diene is reported by Winternitz and Diaz to be at λ 233 (log ε 4·53) as compared with our value of λ 267 mμ (log ε 3·8). Absorption at λ 233 mμ is recorded [1] for the simple diene, 1-1′-acetoxyvinylcyclohexene, and in view of the discussion above it appears probable that cross conjugation with a phenyl group would alter this value, as the ultraviolet absorption maxima of the chromophores C=C–C=C and C=C–C=O are similar (cf. Gillam and Stern, " An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Edward Arnold and Sons, London, 1954).

Experimental

3,4-Dihydro-1-naphthoic Acid.—Sodium (35 g., 1·5 g.-atoms) was added in small pieces during 4 hr. to a stirred mixture of 1-naphthoic acid (86 g., 0·5 mole) in liquid ammonia (1200 ml.) and ethanol (78·2 g., 1·7 moles), contained in a Dewar vessel. The characteristic blue colour of sodium in liquid ammonia was not observed until towards the end of the addition. At this stage the reaction mixture became thick, and liquid ammonia was added to replace loss by evaporation. After being stirred for a further 3 hr. the mixture was left overnight under a stream of nitrogen. A solution of ammonium chloride (108 g.) in water (200 ml.) was then

[13] Jones, *J. Amer. Chem. Soc.*, 1941, **63**, 313.
[14] Ansell, Brooks, and Knights, *J.*, 1961, 212.

added and a fast stream of nitrogen passed through the mixture to expel excess of ammonia. 5N-Hydrochloric acid was added to bring the solution to pH 8, the hot solution was filtered (charcoal), the filtrate made strongly acid with hydrochloric acid, and the precipitated crude 1,4-dihydronaphthoic acid filtered off. The latter was dissolved in the minimum volume of dilute ammonia solution and treated with a saturated aqueous barium chloride until no further precipitation occurred. The precipitate (containing barium 1-naphthoate; cf. ref. 15) was filtered off and the filtrate, cooled in ice, was stirred and slowly acidified with 6N-hydrochloric acid. The granular buff-coloured precipitate was filtered off and washed with water. A sample of the acid, dried and recrystallised from light petroleum (b. p. 60—80°), had m. p. *ca.* 75° [recorded m. p.s for 1,4-dihydronaphthoic acid, 75° (ref. 3, 16), 91° (ref. 15, 17), and 86° (ref. 18)]. A solution of the remainder of the above acid 10% aqueous potassium hydroxide (850 ml.) was boiled for 1 hr. The cold solution was then filtered and adjusted to pH 8 by the addition of 6N-hydrochloric acid and filtered hot (charcoal). The filtrate, cooled in ice, was slowly acidified with 6N-hydrochloric acid. The precipitated solid was filtered off, washed with water, and dissolved in benzene. The residual water was separated from the benzene solution which was then evaporated to a small bulk. Addition of light petroleum (b. p. 60—80°) precipitated 3,4-dihydro-1-naphthoic acid (50 g.), m. p. 115—119°. Sowinski [16] and Birch [3] record m. p. 112°; Fieser [5] records m. p. 120—121°.

3,4-*Dihydro*-1-*naphthoyl Chloride*.—A mixture of 3,4-dihydro-2-naphthoic acid (155 g.) and thionyl chloride (250 ml.) was heated under reflux for 20 min. and then distilled to yield, after removal of excess of thionyl chloride, 3,4-dihydronaphthoyl chloride (159 g.), b. p. 113—114°/0·4 mm. The derived amide had m. p. 187—188° (after crystallisation from methanol) (Found: C, 76·0; H, 6·5; N, 8·2. Calc. for $C_{11}H_{11}NO$: C, 76·3; H, 6·4; N, 8·1%). Birch and Robinson [6] record b. p. 174°/14 mm., amide (not analysed) m. p. 128°. Ranedo [7] records b. p. 206°/65 mm., amide m. p. 185°.

1-*Acetyl*-3,4-*dihydronaphthalene*.—Anhydrous cadmium chloride (120 g.) was added to an ice-cold solution of methylmagnesium bromide (from magnesium 30 g.) in ether (500 ml.). The mixture was stirred and heated under reflux until it no longer gave a positive Gilman reaction (*ca.* 30 min.), and the ether then rapidly distilled off, leaving a partially solid residue. Dry benzene (500 ml.) was then added and distillation continued until the vapour temperature rose to *ca.* 70°. More benzene (50 ml.) was added and then to the vigorously stirred ice-cold solution was added during 10 min., a solution of 3,4-dihydro-1-naphthoyl chloride (155 g.) in benzene (200 ml.). After a short induction period the mixture became yellow and an exothermic reaction ensued, cooling being necessary to maintain a gentle reflux rate. Stirring was continued for 1¼ hr. after the exothermic reaction had ceased. The mixture was then poured on ice and 2N-hydrochloric acid, the benzene layer separated, and the aqueous layer extracted with ether. The combined organic solutions were washed with saturated brine and dried ($MgSO_4$). Distillation gave, after removal of the solvent, 1-acetyl-3,4-dihydronaphthalene (97 g.), b. p. 108—109°/0·09 mm., n_D^{17} 1·5891, $\lambda_{max.}$ 278 mμ (log ε 3·68) (Found: C, 83·4; H, 7·1. Calc for $C_{12}H_{12}O$: C, 83·7; H, 7·0%).

The derived 2,4-*dinitrophenylhydrazone* (red needles from benzene–alcohol) had m. p. 156—157°, $\lambda_{max.}$ (in cyclohexane) 360, 261 mμ (log ε 4·4 and 4·3) (Found: C, 61·3; H, 4·9; N, 15·9. $C_{18}H_{16}N_4O_4$ requires C, 61·4; H, 4·6; N, 15·9%). Chromatography of the residue from the mother-liquors from the foregoing crystallisation in benzene–light petroleum gave a further amount of the 2,4-dinitrophenylhydrazone, together with a small amount of an isomeric orange-yellow compound (prisms from benzene–light petroleum), m. p. 128—129°, $\lambda_{max.}$ (in cyclohexane) 352, 258 mμ (log ε 4·4, 4·3) (Found: C, 61·6; H, 4·5; N, 15·9%). The derived semicarbazone (needles from methanol) had m. p. 195—202°. The m. p. of this compound was dependent on the heating conditions, and the recorded value was obtained by heating from 180° (initial bath-temperature) at 2° per min. (Found: C, 68·1; H, 6·5; N, 18·3. Calc. for $C_{13}H_{15}N_3O$: C, 68·1; H, 6·6; N, 18·3%).

Birch and Robinson [6] record b. p. 165°/11 mm. [2,4-dinitrophenylhydrazone (not analysed), orange-red prisms, m. p. 119—120°; semicarbazone, m. p. 208°].

1-1′-*Acetoxyvinyl*-3,4-*dihydronaphthalene*.—1-Acetyl-3,4-dihydronaphthalene (92 g.) was

[15] Baeyer, *Annalen*, 1891, **266**, 175.
[16] Sowinski, *Ber.*, 1891, **24**, 2355.
[17] Rupe, *Annalen*, 1903, **327**, 186.
[18] von Auwers and Möller, *J. prakt. Chem.*, 1925, **109**, 144.

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added to a boiling mixture of isopropenyl acetate (1050 ml.) and toluene-*p*-sulphonic acid (9·5 g.). The mixture was slowly distilled through a 36″ column packed with Fenske helices. After 4 hr. 27 g. of acetone had been removed, more isopropenyl acetate (100 ml.) was added, and the distillation was continued overnight. The residual liquid was then concentrated to half-bulk by distillation, cooled, and then diluted with an equal volume of ether, washed with 10% aqueous sodium hydrogen carbonate and saturated brine, and dried ($MgSO_4$). The solution was distilled under reduced pressure (vapour temperature up to 40°) and the residue distilled to yield, after a small forerun, 1-1′-*acetoxyvinyl*-3,4-*dihydronaphthalene* (80 g.), b. p. 116—118°/1 × 10^{-2} mm., n_D^{14} 1·5720, $\lambda_{max.}$ 219, 267 mμ (log ε 4·29, 3·8) (Found: C, 78·7; H, 6·8%; *M*, 198. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·6%; *M*, 214). Treatment with Brady's reagent gave a derivative identical with the " red " derivative obtained from the parent ketone.

4-*Acetoxy*-1,2,3,9,10,11-*hexahydrophenanthrene*-1,2-*dicarboxylic Anhydride*.—A solution of the above acetoxy-diene (2·2 g.) and maleic anhydride (1·0 g.) in dry thiophen-free benzene was left at room temperature for 4 days and then boiled under reflux for 1½ hr. and the solvent removed under reduced pressure. The residue readily solidified and was washed with ether and crystallised from ether–methylene chloride to yield 4-*acetoxy*-1,2,3,9,10,11-*hexahydrophenanthrene*-1,2-*dicarboxylic anhydride* (1·7 g.), m. p. 169—170° (Found: C, 69·2; H, 5·2%; *M*, 312. $C_{18}H_{16}O_5$ requires C, 69·2; H, 5·2%; *M*, 329). Hydrolysis of this anhydride with boiling water gave the parent *acid*, m. p. 220—227° (with effervescence) (bath initially at 210°), $\lambda_{max.}$ 252 mμ (log ε 4·1) (Found: C, 65·0; H, 5·4. $C_{18}H_{18}O_6$ requires C, 65·4; H, 5·5%). Treatment of this acid with diazomethane in chloroform converted it into the methyl ester which with Brady's reagent (prepared in methanol) gave *dimethyl* 1,2,3,4,9,10,11,12-*octahydro*-4-*oxophenanthrene*-1,2-*dicarboxylate* 2,4-*dinitrophenylhydrazone* as yellow needles (from benzene), m. p. 209—210°, $\lambda_{max.}$ (in EtOH) 363, 263 mμ (log ε 4·2, 4·0) (Found: C, 58·2; H, 4·8; N, 11·3. $C_{24}H_{24}N_4O_8$ requires C, 58·1; H, 4·9; N, 11·3%).

11-*Acetoxy*-1,4,5,6,12,13,14,15-*octahydro*-1,4-*dioxochrysene*.—A solution of the acetoxydiene (8·8 g.) and *p*-benzoquinone (4·0 g.) in benzene (100 ml.) containing a little quinol was heated under reflux for 8 hr. after which the solvent was removed under reduced pressure. The residual solid (5·0 g.) was washed with a little ether and crystallised successively from benzene and methanol, to yield 11-*acetoxy*-1,4,5,6,12,13,14,15-*octahydro*-1,4-*dioxochrysene*, m. p. 175—185° (flocculent needles). Further recrystallisation did not improve the m. p. The product gave no colour with ethanolic ferric chloride, and its infrared spectrum showed no absorption in the hydroxyl region (Found: C, 74·3; H, 5·9%; *M*, 327. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6%; *M*, 322).

Degradation of 11-*Acetoxy*-1,4,5,6,12,13,14,15-*octahydro*-1,4-*dioxochrysene*.—The above adduct (2 g.) was boiled with a 4 : 1 mixture (20 ml.) of ethanol and 10% hydrochloric acid for 8 hr. The mixture was then evaporated under reduced pressure, and the residue was heated with 5% palladium–charcoal (1 g.) at 320° for 5 hr. during which a small amount of chrysene sublimed. The whole of the reaction mixture was mixed with zinc powder (2 g.), sodium chloride (2 g.), and anhydrous zinc chloride (1 g.), and covered with an equal volume of zinc powder. The latter was heated to dull redness, and the mixture then heated to the same temperature. The sublimate which collected in the cool part of the tube was collected, boiled with dilute sodium hydroxide solution, and crystallised from benzene and aqueous acetic acid, giving chrysene (0·3 g.), m. p. and mixed m. p. 250—252° (recorded [19] m. p. 254).

Reaction of 1-1′-*Acetoxyvinyl*-3,4-*dihydronaphthalene with* 2,6-*Xyloquinone*.—A solution of the diene (17·1 g.), 2,6-xyloquinone (8·0 g.), and quinol (0·12 g.) in absolute ethanol (120 ml.) was heated under reflux for 24 hr., and then evaporated at 15 mm. The residue, on treatment with light petroleum (b. p. 60—80°) and ether, gave 11-*acetoxy*-1,4,4a,4b,5,6,12,12a-*octahydro*-xx-*dimethyl*-1,4-*dioxochrysene* (5·5 g.), m. p. 121—122·5°. Heating for 50 hr. did not improve the yield, and a lower yield was obtained with benzene as the solvent. The product exists in two forms; in some experiments the crude material had m. p. 146—149°. Recrystallisation of either form gave pale yellow needles, m. p. 123—125°, $\lambda_{max.}$ (in cyclohexane) 241 mμ (log ε 4·4) (Found: C, 75·3; H, 6·4%; *M*, 330. $C_{22}H_{22}O_4$ requires C, 75·4; H, 6·3%; *M*, 350).

Degradation of the above adduct. The above adduct (4·7 g.) was reduced twice with lithium aluminium hydride (1·3 g.), and the product heated with potassium hydrogen sulphate (11 g.) as described [18] for 9-acetoxy-$\Delta^{2,9(14)}$-decahydro-1,4-dioxophenanthrene. The dehydrated material (3·0 g.) was heated with selenium (13 g.) at 350° for 24 hr. The cold residue was extracted

[19] Baxter and Hale, *J. Amer. Chem. Soc.*, 1937, **59**, 506.

with benzene, and the extract filtered through a short column of alumina (Peter Spence Type H) and then evaporated. The residual oil (2 g.), on treatment with benzene and alcohol, partially solidified. The solid was filtered off. The liquid product on treatment with a saturated alcoholic solution of picric acid gave a red picrate (m. p. 170—176° after recrystallisation), which on treatment with ammonia gave the parent hydrocarbon which was combined with the solid previously obtained. Recrystallisation of this material from ethanol and then light petroleum gave a compound, m. p. 173—175° (mixed m. p. with 3-methylchrysene 161—168°) which from its ultraviolet absorption spectrum is considered to be a *dimethylchrysene* (Found: C, 92·6; H, 6·2. $C_{20}H_{16}$ requires C, 93·7; H, 6·3%).

4-Methyl-1-(2-1′-naphthylethyl)cyclohexanol.—A solution of 4-methylcyclohexanone (31 g.) in ether (30 ml.) was added slowly to a stirred ice-cold solution of the Grignard reagent prepared from 2-1′-naphthylethyl chloride (48 g.) and magnesium (6 g.) in ether (130 ml.). After the addition the mixture was stirred for 1 hr. at room temperature, left overnight, and then poured on ice and ammonium chloride. The aqueous layer was extracted with ether. Evaporation, at 100°/14 mm., of the dried ($MgSO_4$) combined extracts gave crude *4-methyl-1-(2-1′-naphthylethyl)cyclohexanol* (47 g.). A redistilled sample (b. p. 198—200°/0·5 mm.) solidified and had m. p. 68—69° after crystallisation from light petroleum (b. p. <40°) (Found: C, 84·4; H, 8·7. $C_{19}H_{24}O$ requires C, 85·0; H, 9·0%).

3-Methylchrysene.—The above crude alcohol was heated with glacial acetic acid (200 ml.) and concentrated sulphuric acid (20 ml.) on a steam-bath for 1 hr. with stirring, cooled, diluted with water, and extracted with benzene. The extract was washed with 85% sulphuric acid and then 10% sodium carbonate solution, dried ($MgSO_4$), and evaporated. Distillation of the residue (from sodium) at 0·5 mm. gave a colourless syrup (11 g.). A portion (4 g.) of the latter was heated with selenium (10 g.) at 300—310° for 12 hr. The cold residue was extracted with benzene. The residue obtained on evaporation of the solvent was crystallised from benzene–alcohol and sublimed (220°/0·5 mm.), to yield 3-methylchrysene, m. p. 173·5—174·5°. The derived picrate (orange needles from alcohol) had m. p. 165—166°. Wilds [20] records m. p.s 172·5—173·5° and 166—167·5° respectively.

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Mile End Road, London, E.1. [*Received, May 9th,* 1960.]

[20] Wilds and Shunk, *J. Amer. Chem. Soc.*, 1943, **65**, 469.

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37. *Reduced Cyclic Compounds. Part XI.* The Cyclisation of ω-Arylalkenoic Acids.*

By M. F. Ansell and J. W. Ducker.

Cyclisations of 8-phenyl- and 8-*m*-methoxyphenyl-*trans*-oct-5-enoic acid and 7-phenylhept-4-enoic acid by various reagents are reported. Preparations of the two last-named acids are described.

It has been shown [1] that 8-phenyl-*trans*-oct-5-enoic acid (II; R = H) is converted into 1,2,3,7,8,9,10,10a-octahydro-7-oxocyclohepta[*de*]naphthalene (I) by the action of polyphosphoric acid and into 1,2,3,4,4a,9,10,10a-octahydro-1-oxophenanthrene (IV; R = H) by the action of aluminium chloride on the derived acid chloride. The use of alternative reagents in the latter reaction is now reported and the reaction has been applied to the cyclisation of 8-*m*-methoxyphenyl-*trans*-oct-5-enoic acid and 7-phenylhept-4-enoic acid. The latter has also been cyclised with polyphosphoric acid.

It was considered that the yield of ketone (IV; R = H) from the acid (II; R = H) would parallel the ease of formation of the derived acylium ion. Thus it is known, for

* Part X, preceding paper.

[1] Ansell and Brown, *J.*, 1958, 3956.

example, that acetylium complexes are more ionic than benzoylium complexes and the former give the higher yields in acylation reactions.[2] Acylium ions are conveniently obtained from mixed anhydrides, the polarity of which ranges from the covalent acyl trifluoroacetates,[3] *via* the acyl perchlorates [4] which are largely ionised even in non-polar solvents, to the purely ionic tetrafluoroborates.[5] These mixed anhydrides are readily prepared by the action of the silver salt of the strong acid on an acyl halide. Thus those silver salts which have been used [6] to promote the intramolecular acylation of ω-arylalkanoyl chlorides, may be used to promote the intramolecular acylation of suitably constituted ω-arylalkenoyl chlorides. The accompanying Table shows the results obtained with 8-phenyl-*trans*-oct-5-enoic acid.

Cyclisation of 8-*phenyl*-trans-*oct*-5-*enoyl chloride.*

Cyclising reagent	Solvent	Product (% yield) (IV; R = H)	(III; R = H)	Lactone
$CF_3 \cdot CO_2Ag$	Et_2O			34
$C_3F_7 \cdot CO_2Ag$	Et_2O		10	
$AgClO_4$	$MeNO_2$	30		28
$AgBF_4$	Et_2O		10	18
$AgBF_4$	$MeNO_2$	36		16
$CH_3 \cdot CO \cdot BF_4$	$CHCl_3$	26		17
$CH_3 \cdot COBF_4$ *	$CHCl_3$	45		14
$AlCl_3$ †	CS_2	17		

* On the acid. † See ref. 1.

From the Table it can be seen that, of the silver salts, the perchlorate and tetrafluoroborate are the most effective. However, the nature of the solvent is important: thus, silver tetrafluoroborate in ether produces 2-phenethylcyclohex-2-enone (III; R = H) but in the more polar nitromethane " double cyclisation " to the octahydrophenanthrone (IV; R = H) occurs. Cyclisation of the free acid (II; R = H) with acetyl tetrafluoroborate gave better yields than those obtained with the acid chloride, although acetyl tetrafluoroborate is known [5b] to be an effective acetylating agent.

It is evident that the reaction:

$$\text{(II)}\quad R{\cdot}CO_2H + AcBF_4 \rightleftharpoons AcOH + R{\cdot}CO^+BF_4^- \longrightarrow \text{(IV)}$$

competes very favourable with the acetylation. A similar absence of acetylation is reported by Seel [5a] in the formation of triphenylmethyl tetrafluoroborate from triphenylmethyl chloride and acetyl tetrafluoroborate.

In the cyclisations in which the tricyclic ketone (IV) was formed the product was identical with that obtained by Ansell and Brown,[1] who assigned to it a *trans*-configuration on the basis of the known [7] preferential stability of the *trans*-configuration in the *as*-octahydrophenanthrene series. However, an apparently identical ketone, to which has been assigned a *cis*-configuration, has been obtained by reduction of the unsaturated ketone (V) with lithium in liquid ammonia.[8] Thus the stereochemistry of the ketone obtained in the present work is not, at present, certain.

The infrared spectrum of the lactonic material from these cyclisations showed absorption consistent with its having a six-membered lactone ring and a monosubstituted benzene ring, and was therefore considered to be the lactone of 5-hydroxy-8-phenyloctanoic acid.

[2] Seel and Bauer, *Z. Naturforsch.*, 1947, **2b**, 397; Smorganzkii, *J. Gen. Chem. U.S.S.R.*, 1951, **21**, 723; Cauquil, H. Barrera, and R. Barrera, *Bull. Soc. chim. France*, 1953, 1111.
[3] Bourne, Randles, Stacey, Tatlow, and Tedder, *J. Amer. Chem. Soc.*, 1954, **76**, 3206.
[4] Burton and Prail, *J.*, 1950, 2034.
[5] (*a*) Seel, *Z. anorg. Chem.*, 1943, **250**, 331; (*b*) Olah and Kuhn, *Chem. Ber.*, 1956, **89**, 866; (*c*) Susz and Wuhrmann, *Helv. Chim. Acta*, 1957, **40**, 722.
[6] Burton and Munday, *J.*, 1957, 1718.
[7] Cook, McGinnis, and Mitchell, *J.*, 1944, 286.
[8] Dr. Herchel Smith, personal communication.

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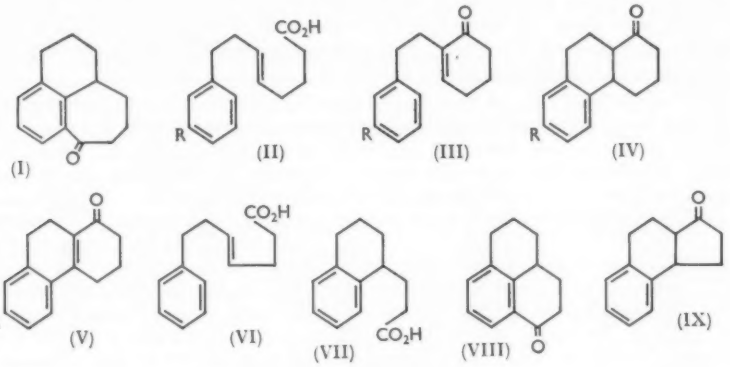
Cyclisation of 8-*m*-methoxyphenyl-*trans*-oct-5-enoic acid (II; R = MeO) was accomplished in a low yield by the action of silver perchlorate or tetrafluoroborate on the acid chloride. The product was pure *trans*-1,2,3,4,4a,9,10,10a-octahydro-7-methoxy-1-oxophenanthrene (IV; R = MeO), identical with that obtained [9] by reduction of the ketone (V; R = MeO) followed by epimerisation. The infrared spectrum of crude cyclisation product gave no indication of the presence of the *cis*-isomer, but showed the presence



of a small amount of an αβ-unsaturated ketone, presumably 2-3′-methoxyphenethylcyclohex-2-enone (III; R = MeO). The infrared spectrum of the lactonic cyclisation product showed absorption consistent with a 6-membered lactone and a 1,3-disubstituted benzene ring.

Cyclisation of 7-phenylhept-4-enoic acid (VI) with polyphosphoric acid occurred, as expected, to yield 2,3,3a,4,5,6-hexahydroperinaphthen-1-one (VIII), presumably *via* the bicyclic acid (VII) which is known [10] to cyclise in this manner. When, however, the phenylheptenoyl chloride was cyclised with aluminium chloride, silver perchlorate, or silver tetrafluoroborate, the known [11] 1,2,3,3a,4,5-hexahydrobenz[*e*]indan-3-one (IX) was obtained in low yield, together with a trace of an αβ-unsaturated ketone, 2-phenethylcyclopent-2-enone. This constitutes the first example of the formation of a five-membered ring in a "double cyclisation," as Ansell and Brown [1] could not cyclise *trans*-7-1′naphthylhept-4-enoic acid in this way. From the heterogeneous lactonic cyclisation product a solid was isolated whose infrared spectrum showed absorption characteristic of a 6-membered lactone and a monosubstituted benzene, and was therefore 5-hydroxy-7-phenylheptanoic lactone. The remaining liquid lactonic material showed, in addition to the characteristic absorption of the solid lactone, absorption characteristic of a five-membered lactone, and was therefore a mixture of the solid lactone and 4-hydroxy-6-phenylhexanoic lactone.

Of the acids described above, the preparation of 8-phenyl-*trans*-oct-5-enoic acid has been previously described.[1] The 8-*m*-methoxyphenyl-*trans*-oct-5-enoic acid was prepared in an analogous manner from 3′-methoxyphenethyl chloride. The report [12] that the preparation of this chloride by the action of thionyl chloride in the presence of pyridine on the parent alcohol gives inconsistent results has been confirmed and we have prepared the chloride by the action of lithium chloride on the corresponding toluene-*p*-sulphonate. An attempt to utilise 3′-methoxyphenethyl bromide was unsuccessful as this compound forms 1,4-di-(*m*-methoxyphenyl)butane to a considerable extent during the preparation of the

[9] Birch, Smith, and Thornton, *J.*, 1957, 1339.
[10] W. S. Johnson, H. C. E. Johnson, and Peterson, *J. Amer. Chem. Soc.*, 1945, **67**, 1360.
[11] Mathieson, *J.*, 1953, 3248.
[12] Bergmann and Weizmann, *J. Org. Chem.*, 1939, **4**, 266.

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derived Grignard reagent (cf. ref. 13). 7-Phenylhept-4-enoic acid was prepared from 6-phenylhex-3-en-1-ol [14] by carboxylation of the Grignard reagent derived from the corresponding chloride.

The preparation of 2-phenethylcyclohex-2-enone by the general method of Born, Pappo, and Szmuzkovicz [15] is described.

Experimental

Refractive indices were taken at 20°.

1-*Chloro*-6-*phenylhex*-3-*ene*.—Thionyl chloride (36 g., 0·3 mole) was added in *ca.* 30 min. to a stirred, boiling solution of 6-phenylhex-3-en-1-ol [14] (51 g., 0·27 mole) and pyridine (0·5 ml.) in benzene (350 ml.). The mixture was then boiled until vigorous evolution of gas ceased, cooled, and poured on ice, and the organic layer was separated, washed with water, saturated sodium hydrogen carbonate solution, and water, dried ($MgSO_4$), and evaporated. Distillation gave 1-*chloro*-6-*phenylhex*-3-*ene* (42 g., 74%), b. p. 76—80°/0·1 mm., n_D 1·5273 (Found: Cl, 18·4. $C_{12}H_{15}Cl$ requires Cl, 18·2%).

7-*Phenylhept*-4-*enoic Acid*.—This *acid* was prepared from the above chloride by the method described [1] for 8-phenyloct-5-enoic acid, a 75% yield being obtained on an 0·2-molar scale. The product had b. p. 100—110°/0·02 mm., n_D 1·5216 (Found: C, 76·2; H, 8·0. $C_{13}H_{16}O_2$ requires C, 76·4; H, 7·9%). The derived acid chloride, prepared as for 8-phenyloct-5-enoyl chloride,[1] resinified on distillation and was not obtained analytically pure.

3′-*Methoxyphenethyl Chloride*.—3′-Methoxyphenethyl toluene-*p*-sulphonate [16] (1140 g., 3·7 moles) was added to a warm (60°) stirred solution of lithium chloride (210 g., 4·9 moles) in 2-ethoxyethanol (2 l.), and the mixture heated on a steam-bath for 4 hr. and then evaporated under reduced pressure. Enough water (*ca.* 1 l.) was added to dissolve the precipitated lithium salts. The organic layer was separated and the aqueous layer extracted with ether (2 × 300 ml.). Distillation of the dried ($MgSO_4$) combined organic material gave 3′-methoxyphenethyl chloride (514 g., 76%), b. p. 86—87°/0·4 mm., n_D 1·5332 (Found: C, 63·7; H, 6·6; Cl, 20·6. Calc. for $C_9H_{11}ClO$: C, 63·4; H, 6·5; Cl, 20·7%) (lit.,[13] b. p. 85—87°/1·5 mm.).

cis- *and* trans-3-*Chlorotetrahydro*-2-3′-*methoxyphenethylpyran*.—This *compound*, b. p. 130—162°/0·4 mm., n_D 1·5312—1·5350 (Found: Cl, 13·6. $C_{14}H_{19}ClO_2$ requires Cl, 13·9%), was prepared (94%) from 3′-methoxyphenethylmagnesium chloride (2·65 moles) and 2,3-dichlorotetrahydropyran (2·0 moles) as described [11] for 3-chlorotetrahydrophenethylpyran.

trans-7-3′-*Methoxyphenylhept*-4-*en*-1-*ol*.—This *alkenol*, b. p. 132—137°/0·2 mm., n_D 1·5273 (Found: C, 76·1; H, 9·4. $C_{14}H_{20}O_2$ requires C, 76·3; H, 9·1%), was prepared (50% on a 2-molar scale) from the above chloro-ether as described [14] for *trans*-7-phenylhept-4-en-1-ol. The derived α-*naphthylurethane* [tablets from light petroleum (b. p. 60—80°)] had m. p. 72—73° (Found: N, 3·9. $C_{25}H_{27}O_3N$ requires N, 3·6%).

trans-1-*Chloro*-7-m-*methoxyphenylhept*-3-*ene*.—The above alcohol (110 g., 0·5 mole) was added dropwise to a stirred suspension of toluene-*p*-sulphonyl chloride (95 g., 0·5 mole) in pyridine (62 g.), kept at 20°. The mixture was then poured on ice (200 g.) and extracted with ether (2 × 75 ml.). The extracts were washed with 6N-sulphuric acid (2 × 50 ml.), water (2 × 50 ml.), saturated sodium hydrogen carbonate solution (2 × 50 ml.), and again water (50 ml.) and dried ($MgSO_4$). The crude toluene-*p*-sulphonate left on removal of the solvent was converted into trans-1-*chloro*-7-3′-*methoxyphenylhept*-3-*ene* (105 g., 88%), b. p. 132—136°/0·6 mm., n_D 1·5234 (Found: C, 70·3; H, 7·9; Cl, 14·7. $C_{14}H_{19}ClO$ requires C, 70·4; H, 8·0; Cl, 14·9%), as described above for 3′-methoxyphenethyl chloride.

trans-8-m-*Methoxyphenyloct*-5-*enoic Acid*.—This *acid*, b. p. 174—177°/0·1 mm., n_D 1·5195 (Found: C, 72·3; H, 7·9. $C_{15}H_{20}O_3$ requires C, 72·5; H, 8·0%), was prepared (15% on a 0·38-molar scale) as for 8-phenyl-*trans*-oct-5-enoic acid.[1] This acid was thermally unstable and only a small sample was distilled; the remainder was used in the crude state. The derived acid chloride, prepared as for 8-phenyl-*trans*-oct-5-enoyl chloride decomposed above 60° and was not distilled. The derived *amide* [plates from light petroleum (b. p. 40—60°)] had m. p. 73—74° (Found: C, 72·8; H, 8·7; N, 5·5. $C_{15}H_{21}NO_2$ requires C, 72·8; H, 8·6; N, 5·7%).

[13] Johnson, Bannerjee, Schneider, Gutsche, Shelberg, and Chinn, *J. Amer. Chem. Soc.*, 1952, **74**, 2832.
[14] Ansell and Selleck, *J.*, 1956, 1238.
[15] Born, Pappo, and Szmuszkovicz, *J.*, 1953, 1779.
[16] Nelson and Wollensak, *J. Amer. Chem. Soc.*, 1958, **80**, 6626.

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General Cyclisation Procedure.—A solution of the acid chloride (0·05 mole) in dry solvent (50 ml.) was added to one of the cyclising agent (0·05 mole) in the same solvent (50—60 ml.) at 0°. Silver chloride was immediately precipitated, and the mixture was shaken intermittently at room temperature for 30 min. and then filtered on to crushed ice. The silver chloride was washed with water (20 ml.) and solvent (20 ml.). The aqueous phase was separated and extracted with ether (50 ml.), and the combined organic solutions were washed with saturated sodium hydrogen carbonate solution (2 × 50 ml.), then with water, and dried ($MgSO_4$), and the solvent was removed. The crude product, Girard's reagent P (8 g.), glacial acetic acid (8 ml.), and ethanol (80 ml.) were boiled under reflux for 2 hr.; the mixture was then cooled, and a solution of sodium hydroxide (4·8 g.) in water (400 ml.) added. The mixture was extracted with ether (3 × 100 ml.) to remove non-ketonic material. Concentrated hydrochloric acid (50 ml.) was added to the aqueous phase, which was left at room temperature for 12 hr. and then extracted with ether (4 × 100 ml.). The latter solution was dried ($MgSO_4$) and distilled to yield the ketonic fraction.

Cyclisation of 8-*Phenyl*-trans-*oct*-5-*enoyl Chloride.*—(a) *With silver trifluoroacetate*[17] *in ether* (0·045-*molar scale*). The ketonic product (1·6 g., 19%), b. p. 115—125°/0·1 mm., formed a heterogeneous 2,4-dinitrophenylhydrazone (red crystals and yellow crystals) which could not be separated. The non-ketonic product (3·4 g., 34%), b. p. 136—137°/0·4 mm., n_D 1·5155, was soluble in warm 2N-sodium hydroxide, and its infrared spectrum showed absorption at 5·85, 13·45 and 14·35 μ characteristic of a 6-membered lactone and a monosubstituted benzene. So the product was accepted as 5-*hydroxy*-8-*phenyloctanoic lactone* (Found: C, 77·9; H, 8·5. $C_{14}H_{18}O_2$ requires C, 77·1; H, 8·3%). The lactonic material obtained in the other cyclisations was essentially similar.

(b) *With silver perfluorobutyrate in ether* (0·05-*molar scale*). The ketonic fraction (1 g., 10%), b. p. 108—110°/0·3 mm., n_D 1·5582, was identified as 2-phenethylcyclohex-2-enone. The derived 2,4-dinitrophenylhydrazone had m. p. and mixed m. p. 155—157° (for authentic constants see below).

(c) *With silver perchlorate in nitromethane* (0·035-*molar scale*). The ketonic material (2·1 g., 30%), b. p. 116—118°/0·1 mm., n_D 1·5581, partially solidified to yield 1,2,3,4,5a,9,10,10a-octahydro-1-oxophenanthrene, m. p. and mixed m. p. (with sample of Ansell and Brown's material) 76—77°. Smith[8] reports m. p. 74—77° for the *cis*-isomer. The infrared spectrum of the liquid product showed, in addition to the absorption due to the octahydro-1-oxo-phenanthrene, absorption at 5·95, 13·45, and 14·35 μ as in the spectra of a cyclohex-2-enone and a monosubstituted benzene (attributable to 2-phenethylcyclohex-2-enone). The 2,4-dinitrophenylhydrazone derived either from the liquid before solidification or from the solid product had (after two recrystallisations) m. p. and mixed m. p. 221—224° (lit.,[1] 221—224°). The derived semicarbazone had m. p. and mixed m. p. 218—220° (lit.,[1] 218—219°).

(d) *With silver tetrafluoroborate*[18] *in ether* (80 ml.) (0·046-*molar scale*). The ketonic fraction (0·9 g., 10%), b. p. 134—140°/0·4 mm., n_D 1·5566, was essentially 2-phenethylcyclohex-2-enone (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 115—117°).

(e) *With silver tetrafluoroborate in nitromethane* (50 *ml.*) (0·03-*molar scale*). The ketonic fraction (2·2 g., 36%), b. p. 120—126°/0·2 mm., partially solidified to yield 1,2,3,4,4a,9,10,10a-octahydro-1-oxophenanthrene, m. p. and mixed m. p. 76—77°. The presence of 2-phenethylcyclohex-2-enone in the residual liquid product was detected spectroscopically.

(f) *With acetyl tetrafluoroborate*[18a] *in chloroform* (0·04-*molar scale*) *initially at* −10°, *then* 10 *min. at room temperature.* The properties of the ketonic and the lactonic fraction were as in the previous experiment (see Table for yields).

(g) *With acetyl tetrafluoroborate and the free acid* (0·046-*molar scale*), *as in the previous experiment.* The properties of the ketonic and the lactonic material were as in the previous experiment (see Table for yields).

Cyclisation of 8-m-*Methoxyphenyl*-trans-*oct*-4-*enoic Acid.*—This acid (0·016 mole) was cyclised by the above general method, with silver perchlorate in nitromethane. The crude ketonic material (15%) was dissolved in 4 : 1 light petroleum (b. p. 60—80°)–benzene and adsorbed on fuller's earth. Elution with chloroform gave *trans*-1,2,3,4,4a,9,10,10a-octahydro-7-methoxy-1-oxophenanthrene, m. p. 109—110° after crystallisation from light petroleum (b. p. 60—80°) (lit.,[9] m. p. 111°). The derived 2,4-dinitrophenylhydrazone (yellow tablets

[17] Crawford and Simons, *J. Amer. Chem. Soc.*, 1955, **77**, 2605.
[18] Sharpe, *J.*, 1952, 4538; Clifford and Kongpricha, *J. Inorg. Nuclear Chem.*, 1957, **5**, 76.

from ethanol–chloroform) had m. p. 208—209° (lit.,[19] m. p. 208—209°). The use of silver tetrafluoroborate gave essentially the same result.

The infrared spectrum of the crude material showed absorption at 5·95 μ characteristic of an αβ-unsaturated ketone (2-3′-methoxyphenethylcyclohexene) but no absorption at 11·6 μ characteristic [9] of the *cis*-octahydro-1-oxophenanthrene.

Cyclisation of 7-Phenylhept-4-enoyl Chloride.—(*a*) This was done with aluminium chloride on a 0·05-molar scale as described [1] for the comparable cyclisation of 8-phenyloct-5-enoic acid, followed by treatment with Girard's reagent P as described in the general cyclisation procedure. Distillation of the ketonic product gave essentially 1,2,3,3a,4,5-hexahydrobenz[*e*]indan-3-one (1·5 g., 17%), b. p. 100—107°/0·1 mm. The derived 2,4-dinitrophenylhydrazone (pale orange plates from chloroform–ethanol) had m. p. 214—215°, and the semicarbazone (needles from ethanol) had m. p. 230—231° (both m. p.s after two recrystallisations). Mathieson [11] records b. p. 135—140°/6 mm. and m. p.s 214—215° and 231—235° respectively. The infrared spectrum of the cyclisation product showed absorption at 5·7 and 13·3 μ as in the spectra of 5-membered cycloalkanones and 1,2-disubstituted benzene, together with absorption at 5·9, 13·45, and 14·3 μ as in the spectra of cyclopent-2-enones and monosubstituted benzenes, indicating the presence of 2-phenethylcyclopent-2-enone.

(*b*) Cyclisation with acetyl tetrafluoroborate on a 0·05-molar scale by the above general method gave a 3% yield of unidentified ketonic product, together with a 75% yield of lactonic material, from which a solid separated. The solid was identified as *5-hydroxy-7-phenylheptanoic lactone* [needles from light petroleum (b. p. 40—60°)], m. p. 53—54° (Found: C, 76·4; H, 7·9. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·9%). Its infrared spectrum showed absorption at 5·86, 13·45, and 14·3 μ, characteristic of a 6-membered lactone and a monosubstituted benzene. The residual liquid lactonic material (Found: C, 76·3; H, 7·8%) showed absorption at 5·78, 5·86, 13·45, and 14·3 μ indicative of a mixture of the γ- and δ-lactone. The ketonic material obtained on cyclisation with either silver perchlorate (12% on an 0·03-molar scale) or silver tetrafluoroborate (20% on an 0·025-molar scale) was essentially the same as that obtained with aluminium chloride. In the latter ($AgBF_4$) experiment a mixture of γ- and δ-lactones was also obtained.

Cyclisation of 7-Phenylhept-4-enoic Acid with Polyphosphoric Acid.—A stirred mixture of polyphosphoric acid (30 g.) and 7-phenylhept-4-enoic acid (3 g.) was heated at 60—70° for 20 min. and then rapidly cooled. Ice-water (60 ml.) was added and the mixture extracted with ether (2 × 60 ml.). The ethereal extract was washed with sodium hydrogen carbonate solution (60 ml.) and water (60 ml.), dried ($MgSO_4$), and evaporated to yield crude 2,3,3*a*,4,5,6-hexahydroperinaphthen-1-one (1·9 g., 70%), m. p. 67—70°. One crystallisation (from ethanol) yielded the pure ketone (as laths), m. p. 71—72°. The derived semicarbazone (tablets from ethanol–pyridine) had m. p. 231—232°; the derived oxime (needles from ethanol) had m. p. 161—162°; and the derived *2,4-dinitrophenylhydrazone* (crimson plates from ethanol–chloroform) had m. p. 255—256° (Found: C, 62·4; H, 5·0; N, 15·4. $C_{19}H_{18}N_4O_4$ requires C, 62·3; H, 4·9; N, 15·3%). The recorded constants are: ketone [13] m. p. 69·7—70°, oxime [20] m. p. 159—160°, semicarbazone [13] m. p. 230·5—231·7°.

2-Phenethylcyclohex-2-enone.—A solution of 2-phenethylcyclohexane-1,3-dione [21] (5·5 g.) and toluene-*p*-sulphonic acid monohydrate (0·5 g.) in isobutyl alcohol (10 ml.) and benzene (20 ml.) was heated under reflux for 6 hr., the water formed in the reaction being removed by a Dean and Stark separator. The cold mixture was washed with 5% sodium hydrogen carbonate solution (10 ml.), 5% sodium hydroxide solution (3 × 10 ml.), and water (10 ml.) and dried ($MgSO_4$), the solvent removed, and the residue distilled to yield *3-isobutoxy-2-phenethylcyclohex-2-enone* (4·7 g., 80%), b. p. 131—136°/0·2 mm., m. p. 69—70° (unrecrystallised) (Found: C, 78·8; H, 8·8. $C_{18}H_{24}O_2$ requires C, 79·3; H, 8·8%). A solution of the latter (4·0 g.) in ether (10 ml.) was added to a stirred suspension of lithium aluminium hydride (0·3 g.) in ether at such a rate that steady refluxing was maintained. The mixture was stirred for a further 15 min., then cooled to 0°, and sufficient (*ca.* 25 ml.) of 10% sulphuric acid added to yield two clear phases. The aqueous phase was continuously extracted with ether for 20 hr. Distillation of the combined dried ($MgSO_4$) ethereal solutions gave 2-phenethylcyclohex-2-enone (1·3 g.), b. p. 102—105°/0·4 mm., n_D^{20} 1·5570 (Found: C, 84·0; H, 7·9. Calc. for $C_{14}H_{16}O$: C, 84·0; H, 8·0%). The derived semicarbazone (needles from ethanol) had m. p. 188—189°, and the 2,4-*dinitrophenylhydrazone* (red

[19] Robinson and Walker, *J.*, 1936, 747.
[20] von Braun and Reutter, *Ber.*, 1926, **59**, 1922.
[21] Birch and Smith, *J.*, 1951, 1882; Stetter and Dierichs, *Chem. Ber.*, 1952, **85**, 61.

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laths from ethanol–chloroform) had m. p. 155—157° (Found: C, 62·6; H, 5·4; N, 15·3. $C_{20}H_{20}N_4O_4$ requires C, 63·1; H, 5·3; N, 14·8%). Cohen and Cook [23] record this compound as a highly refractive liquid, b. p. 125—130°/0·7 mm. [semicarbazone, m. p. 188—189°].

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QUEEN MARY COLLEGE, LONDON, E.1. [*Received, May 9th,* 1960.]

[23] Cohen and Cook, *J.*, 1935, 1570.

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38. *The Synthesis of Four Dimethylchrysenes.*

By M. F. ANSELL, G. T. BROOKS, and B. A. KNIGHTS.

Preparations of 1,2-, 3,4-, 3,5-, and 2,12-dimethylchrysene are described.

In connection with another investigation [1] we required to prepare the above named dimethylchrysenes. Tetracyclic precursors (I and III) being available,[2,3] they were treated with methylmagnesium bromide, and the products dehydrogenated with palladium–charcoal to yield 1,2- (II) and 3,4-dimethylchrysene (IV) respectively.

For the synthesis of 3,5- and 2,12-dimethylchrysene, the general route used by Newman [4] was adapted. For the preparation of the 3,5-dimethyl compound benzyl cyanide was alkylated with 4-methylphenethyl chloride (or bromide) to yield 1-phenyl-3-*p*-tolylpropyl cyanide (V; X = CN) which was hydrolysed to the corresponding acid (V; X = CO_2H) which had previously been prepared [5] by reduction of α-phenyl-β-*p*-toluoylpropionic acid. The acid (V; X = CO_2H) readily cyclised in the presence of anhydrous hydrogen fluoride to 7-methyl-2-phenyltetral-1-one (VI). This was converted into the unsaturated acid (VII) by a Reformatsky reaction with isobutyl α-bromopropionate followed by hydrolysis. The position of the double bond in the acid (VII) was assigned by analogy with previous work [4a] and from the similarity of the ultraviolet spectrum to that of *trans*-stilbene. Reduction of this acid (VII) to the saturated acid (VIII) could not be achieved by use of sodium amalgam or by catalytic hydrogenation (cf. ref. 4) but was readily effected with sodium in liquid ammonia (cf. ref. 6).

Cyclisation of the acid (VIII) with anhydrous hydrogen fluoride may give either the hydrochrysene derivative (IX) or the hydroacenaphthene derivative (X). The former would be expected to be the predominant, though not exclusive product, owing to the preferential formation of a six-membered ring.[7] The cyclisation product from the acid (VIII) was not homogeneous. It was reduced, dehydrated, and dehydrogenated and from the products was isolated 3,5-dimethylchrysene (XI) together with some impure material which had an infrared band at 14·25 μ characteristic [8] of a monosubstituted benzene and attributable to the presence of a phenyl-substituted acenaphthene derivative. The formation of an acenaphthene derivative has not previously been observed in cyclisations of this type (cf. ref. 4).

2,12-Dimethylchrysene was prepared by a similar reaction sequence, 4-methylbenzyl cyanide giving successively the cyanide (XII; X = CN), the acid (XII; X = CO_2H), and 2-*p*-tolyltetral-1-one (XIII). The ketone, on condensation with ethyl bromoacetate,

[1] Ansell and Brooks, *J.*, 1960, **1**, 201.
[2] Bachmann and Struve, *J. Org. Chem.*, 1940, **5**, 46.
[3] Wilds and Werth, *J. Org. Chem.*, 1952, **17**, 1149.
[4] Newman, *J. Amer. Chem. Soc.*, (*a*) 1938, **60**, 2947; (*b*) 1940, **62**, 870; (*c*) *ibid.*, p. 2295.
[5] Hidayetulla, Shah, and Wheeler, *J.*, 1941, 111.
[6] Robins and Walker, *J.*, 1957, 4984.
[7] Johnson, "Organic Reactions," Wiley, New York, 1944, Vol. IV, p. 114.
[8] Bellamy, "Infra-red Spectra of Complex Molecules," Methuen, London, 1954.

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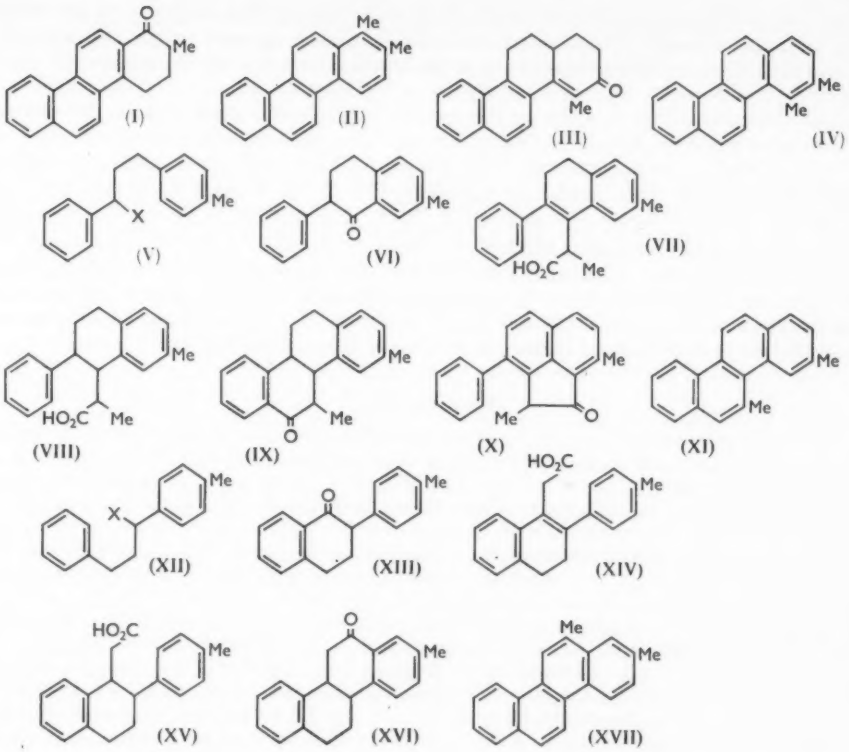

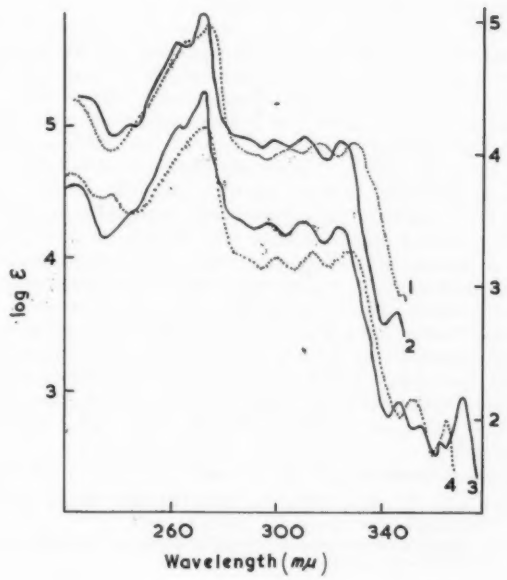

1, 3,4-*Dimethylchrysene.*
2, 1,2-*Dimethylchrysene.*
3, 2,12-*Dimethylchrysene.*
4, 3,5-*Dimethylchrysene.*
Curves 1 *and* 2*—right-hand scale.*

followed by hydrolysis, gave the unsaturated acid (XIV), which was reduced by sodium in liquid ammonia to the saturated acid (XV) and then cyclised to the hydrochrysene derivative (XVI). This cyclisation, as in the analogous cyclisation described above, may proceed in two ways. However, in this case the hydrochrysene (XVI) derivative was almost exclusively formed, although the presence of a second ketonic product, presumably a hydroacenaphthene derivative, was detected. This difference may be due to the fact that in the earlier case the chrysene derivative formed has a methyl group in the sterically hindered 5-position, thus increasing the proportion of the acenaphthene derivative (X) produced. The hydrochrysene derivative (XVI) was readily converted, by treatment with methylmagnesium iodide, followed by dehydrogenation with palladised charcoal, into 2,12-dimethylchrysene. A comparison of the ultraviolet absorption spectra (see Figure) of the above dimethylchrysenes shows that the principal maximum is not resolved when one of the methyl groups is present at either the 4- or the 5-position. A similar lack of resolution is found in the spectra of 4- and 5-monomethylchrysene.[9]

Experimental

1,2-*Dimethylchrysene*.—A solution of 1,2,3,4-tetrahydro-2-methyl-1-oxochrysene [2] (1·4 g.) in benzene (60 ml.) was added to a solution of methylmagnesium iodide [from magnesium (2 g.) and methyl iodide (6·4 ml.)] in ether (100 ml.). The mixture was boiled under reflux for 36 hr., then cooled and treated with water and sufficient 2N-hydrochloric acid to give two phases. The aqueous phase was extracted with benzene, and the combined extracts were washed with water. The residue (1·4 g.) obtained on evaporation of the benzene gave a positive reaction with Brady's reagent. It was boiled with a solution of Girard's reagent P (2·5 g.) in ethanol (40 ml.) and acetic acid (5 ml.) for 45 min. and then cooled, poured into water containing 2N-sodium hydroxide (37 ml.), and extracted with benzene. The non-carbonylic residue obtained on evaporation of the benzene extract was dehydrogenated at 300—310° with 5% palladised charcoal (1 g.). Extraction with benzene, crystallisation of the extracted material from benzene, and sublimation gave **1,2-*dimethylchrysene*** (0·6 g.), m. p. 263—264° (Found: C, 93·7; H, 6·3. $C_{20}H_{16}$ requires C, 93·7; H, 6·3%). The **1,3,5-*trinitrobenzene complex*** (orange-yellow needles from ethanol) had m. p. 196—198° (Found: C, 66·7; H, 4·1; N, 8·4. $C_{26}H_{19}N_3O_6$ requires C, 66·5; H, 4·1; N, 8·9%). The picrate appeared to be unstable and could not be obtained free from the hydrocarbon.

3,4-*Dimethylchrysene*.—A solution of 1,2,3,11,12,13-hexahydro-4-methyl-3-oxochrysene [3] (1 g.) in benzene (22 ml.) was added to one of methylmagnesium iodide [from magnesium (0·5 g.) and methyl iodide (1·6 ml.)] in ether (40 ml.), and the mixture boiled under reflux for 36 hr. The subsequent procedure was as for 1,2-dimethylchrysene. The dehydrogenation product was recrystallised from light petroleum (b. p. 60—80°) and ethanol and then sublimed to yield **3,4-*dimethylchrysene*** (0·6 g.) (needles from light petroleum), m. p. 127·5—128·5° (Found: C, 93·5; H, 6·7%). The ***picrate*** (prepared in benzene; bright red needles from ethanol) had m. p. 133—134° (Found: C, 64·3; H, 3·9; N, 8·7. $C_{26}H_{19}N_3O_7$ requires C, 64·3; H, 4·0; N, 8·7%) and the **1,3,5-*trinitrobenzene complex*** (prepared in benzene; orange-yellow needles from ethanol) had m. p. 166—167° (Found: C, 66·6; H, 4·1; N, 8·3%).

3-*Phenyl*-1-p-*tolylpropyl Cyanide*.—(*a*) 4-Methylbenzyl cyanide [10] (44 g., 0·33 mole) was added during 5 min. to a stirred cooled suspension of sodamide (13 g., 0·33 mole) in dry thiophen-free benzene (165 ml.) under nitrogen, and the mixture was then boiled under reflux for 1 hr. It was then cooled to 0° and phenethyl chloride [11] (22 g., 0·153 mole) added during 2 hr. (stirring). After being stirred for a further 3 hr. at room temperature it was heated under reflux for 30 min., then cooled and 2N-hydrochloric acid (300 ml.) added. The benzene layer was separated, washed with brine, and distilled to yield, after a small fore-run, **3-*phenyl*-1-p-*tolylpropyl cyanide*** (14 g., 40%), b. p. 160—162°/0·09 mm., n_D^{20} 1·5592 (Found: N, 6·25. $C_{17}H_{17}N$ requires N, 6·0%).

(*b*) 4-Methylbenzyl cyanide (120 g.) was added to a stirred suspension of sodamide (from

[9] Jones, *J. Amer. Chem. Soc.*, 1941, **63**, 313; Brode and Patterson, *ibid.*, p. 3252.
[10] Atkinson and Thorpe, *J.*, 1907, **91**, 1697.
[11] Prepared from the corresponding alcohol as described by Ansell and Ducker (preceding paper), for 1-chloro-6-phenylhex-3-ene.

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sodium, 22 g.) in liquid ammonia (600 ml.). Dry toluene (600 ml.) was added and the liquid ammonia distilled off. To the warm, stirred, red suspension was added, during 20 min., phenethyl bromide [12] (195 g.) with intermittent cooling, and the mixture was heated under reflux for 2 hr., then cooled and worked up as in method (*a*), to yield 3-phenyl-1-*p*-tolylpropyl cyanide (83 g., 38%), b. p. 150—160°/0·16—0·2 mm.

1-*Phenyl*-3-p-*tolylpropyl Cyanide*.—This *compound*, b. p. 156—162°/0·05 mm., n_D^{20} 1·5588 (analytical sample, b. p. 152°/0·04 mm., n_D^{20} 1·5598) (Found: N, 5·85. $C_{17}H_{17}N$ requires N, 6·0%), was prepared as for the isomeric cyanide in 33% yield by method (*a*) using benzyl cyanide (0·8 mole) and 4-methylphenethyl chloride [11] (0·7 mole) and method (*b*) (72% yield) using benzyl cyanide (1·3 moles) and 4-methylphenethyl chloride (0·55 mole).

γ-Phenyl-α-p-*tolylbutyric Acid*.—A mixture of 3-phenyl-1-*p*-tolylpropyl cyanide (10 g.), acetic acid (37·5 ml.), concentrated sulphuric acid (7 ml.) and water (5 ml.) was boiled under reflux for 66 hr. Water (10 ml.) was added, the mixture distilled under reduced pressure (water-pump) to remove most of the acetic acid and water, and the residue extracted with benzene and washed with water and saturated sodium carbonate solution. The alkaline washings were acidified with concentrated hydrochloric acid, and the precipitated acid was taken up in benzene. Distillation of the benzene extract gave *γ-phenyl*-α-p-*tolylbutyric acid* (8·0 g., 74%), b. p. 186°/0·1 mm., which solidified. A sample crystallised from light petroleum (b. p. 60—80°) had m. p. 74—76° (Found: C, 80·7; H, 7·3. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%).

α-*Phenyl*-*γ*-p-*tolylbutyric Acid*.—1-Phenyl-3-*p*-tolylpropyl cyanide (10 g.), treated as in the previous experiment, gave α-phenyl-*γ*-*p*-tolylbutyric acid (9·6 g., 88%), b. p. 160—165°/1—1·6 × 10^{-2} mm., which solidified (m. p. 76·5—78° after crystallisation from hexane) (lit.,[5] m. p. 80°).

2-p-*Tolyltetral*-1-*one*.—A solution of *γ*-phenyl-α-*p*-tolylbutyric acid (5 g.) in anhydrous hydrogen fluoride, contained in a Polythene beaker, was left overnight and then diluted with water and extracted with ether. The extract was washed with water and 10% aqueous sodium carbonate solution, dried ($MgSO_4$), and evaporated to yield 2-*p*-tolyltetral-1-one (4·4 g., 94%), m. p. 53—62°. One crystallisation (from methanol) gave the ketone, m. p. 72—74°. The analytical sample had m. p. 73—74° (Found: C, 86·4; H, 6·5. Calc. for $C_{17}H_{16}O$: C, 86·4; H, 6·8%). The 2,4-*dinitrophenylhydrazone* (red needles from ethanol–chloroform) had m. p. 226—227° (Found: N, 13·4. $C_{23}H_{20}N_4O_4$ requires N, 13·5%), and the *semicarbazone* (from ethanol–pyridine) had m. p. 192—194° (Found: N, 14·4. $C_{18}H_{19}N_3O_3$ requires N, 14·3%).

7-*Methyl*-2-*phenyltetral*-1-*one*.—α-Phenyl-*γ*-*p*-tolylbutyric acid (5 g.), treated as in the previous experiment, gave 7-methyl-2-phenyltetral-1-one (4·3 g., 92·5%), m. p. 62—66°. Crystallisation from methanol gave the pure ketone (prisms), m. p. 66—67° (lit.,[5] m. p. 67°). The 2,4-*dinitrophenylhydrazone* (red needles from chloroform) had m. p. 230—231° (Found: N, 13·2. $C_{23}H_{20}N_4O_4$ requires N, 13·5%), and the *semicarbazone* (from benzene–alcohol) had m. p. 234—236° decomp. (Found: N, 14·4. $C_{18}H_{19}NO_3$ requires N, 14·3%).

3,4-*Dihydro*-2-p-*tolyl*-1-*naphthylacetic Acid*.—A stirred mixture of 2-*p*-tolyltetral-1-one (37·5 g.), clean zinc foil (11 g.), ethyl bromoacetate (15 g.), a crystal of iodine, ether (300 ml.), and benzene (300 ml.) was boiled for 4 hr. During this time four additions of zinc foil (total, 44 g.), ethyl bromoacetate (total, 15 g.) and iodine were made at 30-min. intervals. After 2 hours' boiling an exothermic reaction ensued and spontaneous boiling occurred for *ca.* 20 min. At the end of the reaction time the mixture was cooled, and sufficient 2N-hydrochloric acid added to give two phases. The organic layer was separated and the aqueous layer extracted with benzene. Distillation of the combined extracts gave, after removal of the solvent, 42 g. of material, b. p. 180—190°/0·2 mm. The latter was hydrolysed by boiling with a solution of potassium hydroxide (45 g.) in water (250 ml.) and ethanol (250 ml.) for 18 hr. The bulk of the alcohol was removed by distillation under reduced pressure (water-pump) and the residue was extracted with benzene. The aqueous phase was acidified with concentrated hydrochloric acid, and the precipitated oil extracted with benzene. Concentration of the latter extract yielded 3,4-*dihydro*-2-p-*tolyl*-1-*naphthylacetic acid* (19 g.), m. p. 187—192°. Concentration of the mother-liquors gave a further 16·5 g. of the material which when recrystallised from acetic acid gave the acid (8·5 g.), m. p. 185—190°. An analytical sample [prisms from benzene–light petroleum (b. p. 60—80°)] had m. p. 185—191° (Found: C, 82·3; H, 6·4. $C_{19}H_{18}O_2$ requires C, 82·6; H, 6·5%).

α-(3,4-*Dihydro*-7-*methyl*-2-*phenyl*-1-*naphthyl*)*propionic Acid*.—This *acid* was prepared from

[12] Dolique, *Ann. Chim.* (*France*), 1931, **15**, 436.

7-methyl-2-phenyltetral-1-one and isobutyl α-bromopropionate on the same molar scale as in the previous experiment, *via* the intermediate ester (48 g.), b. p. 160—180°/0·2 mm. [yield of crude acid (21 g., 42·4%)], m. p. 150—174°. Crystallisation from ethanol gave the pure acid (13·5 g., 23%), m. p. 169—172° (Found: C, 82·5; H, 6·8. $C_{20}H_{20}O_2$ requires C, 82·2; H, 6·8%), $\lambda_{max.}$ 275 mμ (log ε 4·11) (in EtOH).

1,2,3,4-*Tetrahydro*-2-p-*tolyl*-1-*naphthylacetic Acid*.—Sodium (8 g.) was added in small portions during 5 min. to a stirred solution of 3,4-dihydro-2-*p*-tolyl-1-naphthylacetic acid (6·4 g.) in liquid ammonia (2 l.) and dry tetrahydrofuran (500 ml.). After 10 min. the colour of the solution was destroyed by the addition of propan-2-ol (100 ml.). The ammonia was left to evaporate overnight and the residue then treated with water (250 ml.), made acid with concentrated hydrochloric acid, and extracted with ether. The residue (6 g.) obtained on evaporation of the dried ($MgSO_4$) extract was crystallised from acetic acid (charcoal), to give 1,2,3,4-*tetrahydro*-2-p-*tolyl*-1-*naphthylacetic acid* (4·85 g.), m. p. 148—153°. An analytical sample (crystallised from alcohol) had m. p. 155—158·5 (Found: C, 81·4; H, 7·1. $C_{19}H_{20}O_2$ requires C, 81·4; H, 7·1%), $\lambda_{max.}$ 266 and 273 mμ, $\lambda_{min.}$ 235 and 270 mμ (log ε 2·85, 2·78, 2·37, and 2·68 respectively).

5,6,11,12,15,16-*Hexahydro*-2-*methyl*-12-*oxochrysene*.—The above acid (3·65 g.) was cyclised as for γ-phenyl-α-*p*-tolylbutyric acid. The non-acidic product (3·4 g.; m. p. 129—139°) was recrystallised twice from benzene–alcohol to yield 5,6,11,12,15,16-*hexahydro*-2-*methyl*-12-*oxochrysene* (1·4 g.) as plates, m. p. 140—142° (raised to 143—144° on further recrystallisation) (Found: C, 87·0; H, 6·9. $C_{19}H_{18}O$ requires C, 87·0; H, 6·9%). Its 2,4-*dinitrophenylhydrazone* (from chloroform–alcohol) partially melted at 160—180°, resolidified, and finally melted at 243—246° (decomp.) (Found: C, 67·4; H, 5·2; N, 12·7. $C_{25}H_{22}N_4O_4$ requires C, 67·9; H, 5·0; N, 12·7%). Chromatography, in ether–light petroleum (b. p. 60—80°) on alumina, of the residue obtained from evaporation of the ketone mother-liquors yielded a further 0·7 g. of the required ketone (m. p. 140—142°) together with a small amount of material, m. p. 78—127°, which afforded a red 2,4-dinitrophenylhydrazone, m. p. 145—150° (Found: C, 68·1; H, 5·1; N, 12·4. Calc. for $C_{25}H_{22}N_4O_4$: C, 67·9; H, 5·0; N, 12·7%).

2,12-*Dimethylchrysene*.—A solution of 5,6,11,12,15,16-hexahydro-2-methyl-12-oxochrysene (2·1 g.) in benzene (50 ml.) was added to a stirred solution of methylmagnesium iodide (from magnesium, 2 g.) in ether (40 ml.), and the mixture heated under reflux for 24 hr. The subsequent precedure was as for 1,2-dimethylchrysene (except that treatment with Girard's reagent was not necessary). The dehydrogenation product was sublimed (1·2 g.; m. p. 137—147°) and recrystallised from benzene–light petroleum (b. p. 60—80°), to yield 2,12-*dimethylchrysene*, needles, m. p. 150·5—151·5° (Found: C, 93·4; H, 6·4%). The *picrate* (red needles from benzene) had m. p. 187—188·5° (decomp.) (Found: C, 64·6; H, 3·9; N, 8·6%), and the 1,3,5-*trinitrobenzene complex* (yellow-orange needles from benzene) had m. p. 205—207·5° (Found: C, 66·3; H, 3·7; N, 8·7%).

3,5-*Dimethylchrysene*.—α-(3,4-Dihydro-7-methyl-2-phenyl-1-naphthyl)propionic acid (6·5 g.) was reduced as was 3,4-dihydro-2-*p*-tolyl-1-naphthylacetic acid. The products from two such reactions were combined and recrystallised from light petroleum (b. p. 60—80°) to yield α-(1,2,3,4-tetrahydro-7-methyl-2-phenyl-1-naphthyl)propionic acid (2·7 g.), m. p. 113—123°, $\lambda_{max.}$ 270, 278 (log ε 2·81, 2·81). Further recrystallisation did not raise the m. p. All of this acid was cyclised as for γ-phenyl-α-*p*-tolylbutyric acid by use of anhydrous hydrogen fluoride (35 ml.). The non-acidic product (2·2 g.), m. p. 65—95°, was fractionally crystallised from ethanol to yield material (1·3 g.), m. p. 95—100°, and material (0·3 g.), m. p. 78—83°. The former fraction (1·2 g.) was dissolved in dry ether (50 ml.), boiled with lithium aluminium hydride (2 g.) in ether (100 ml.) for 2 hr., and then cooled. Excess of hydride was decomposed by water, and the ether layer was decanted. Evaporation of the dried ($MgSO_4$) extract gave a partially solid, non-ketonic product which was heated with powdered fused potassium hydrogen sulphate at 180—200° for 45 min. in an atmosphere of nitrogen. The product was treated with water and extracted with benzene. The residue obtained on removal of the solvent was heated with 5% palladised charcoal (1 g.) at 300—320° for 4 hr. The product was extracted with benzene, the catalyst removed, and the solvent evaporated. The residual partly solid product was distilled (150—180°/0·1 mm.). The partly solid distillate was washed with cold ether (extract A) and then crystallised from benzene–ethanol and from light petroleum (b. p. 60—80°), to yield 3,5-*dimethylchrysene*, m. p. 126—128·5° (Found: C, 93·7; H, 6·3%). The *picrate* (red needles from benzene) had m. p. 150—154° (Found: N, 8·7%).

XUM

The liquid dehydrogenation product from extract A was chromatographed in light petroleum (b. p. <40°) on alumina but no further solid was obtained. The infrared spectrum of the liquid product showed absorption at 12·03 and 14·25 μ, indicating a free phenyl group.

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39. *The Influence of the Nitro-group upon Side-chain Reactivity. Part I. The Reaction between 4-Nitrobenzyl Chloride and Alkali.*

By SAMIR B. HANNA, YOUSSEF ISKANDER, and (in part) YOUSSEF RIAD.

The reaction between 4-nitrobenzyl chloride and alkali in aqueous acetone or aqueous dioxan gives 4,4′-dinitrostilbene. The kinetic form, the effect of added aldehydes, and the effect of deuterium in the starting material have been studied. *p*-Nitrophenylmethylene is accepted as an intermediate.

WHEN 4-nitrobenzyl chloride is hydrolysed by alkali in water, it gives the normal product, 4-nitrobenzyl alcohol,[1] but reaction in aqueous alcohol, acetone, or dioxan gives the 4,4′-dinitrostilbene.[2] This abnormal behaviour was investigated by Bergmann and Hervey,[3] who proposed a mechanism involving the free biradical *p*-nitrophenylmethylene:

$$O_2N{\cdot}C_6H_4{\cdot}CH_2Cl + NaOH \longrightarrow O_2N{\cdot}C_6H_4{\cdot}CH{:} + NaCl + H_2O \quad (1a)$$

$$2O_2N{\cdot}C_6H_4{\cdot}CH{:} \longrightarrow O_2N{\cdot}C_6H_4{\cdot}CH{:}CH{\cdot}C_6H_4{\cdot}NO_2 \quad (1b)$$

They based their proposal on the fact that in presence of carbonyl compounds the reaction would be diverted to the formation of epoxides, *e.g.*:

$$O_2N{\cdot}C_6H_4{\cdot}CH{:} + Ph{\cdot}CHO \longrightarrow O_2N{\cdot}C_6H_4{\cdot}\underset{\diagdown\,O\,\diagup}{CH{-}CH}Ph \quad (1c)$$

Hahn,[4] and Kleucker,[5] on the other hand, considered that the reaction involved nucleophilic displacement by a carbanion, thus:

$$O_2N{\cdot}C_6H_4{\cdot}CH_2Cl + OH^- \rightleftharpoons O_2N{\cdot}C_6H_4{\cdot}\bar{C}HCl \quad (2a)$$

$$O_2N{\cdot}C_6H_4{\cdot}\bar{C}HCl + O_2N{\cdot}C_6H_4{\cdot}CH_2Cl \longrightarrow O_2N{\cdot}C_6H_4{\cdot}CHCl{\cdot}CH_2{\cdot}C_6H_3{\cdot}NO_2 + Cl^- \quad (2b)$$

$$O_2N{\cdot}C_6H_4{\cdot}CHCl{\cdot}CH_2{\cdot}C_6H_4{\cdot}NO_2 \longrightarrow HCl + O_2N{\cdot}C_6H_4{\cdot}CH{:}CH{\cdot}C_6H_4{\cdot}NO_2 \quad (2c)$$

In this case the intercepting process would be:

$$O_2N{\cdot}C_6H_4{\cdot}\bar{C}HCl + Ph{\cdot}CHO \longrightarrow O_2N{\cdot}C_6H_4{\cdot}\underset{Cl}{\overset{O^-}{CH{\cdot}CH}}Ph \quad (2d)$$

$$O_2N{\cdot}C_6H_4{\cdot}\underset{Cl}{\overset{O^-}{CH{\cdot}CH}}Ph \longrightarrow O_2N{\cdot}C_6H_4{\cdot}\underset{\diagdown\,O\,\diagup}{CH{-}CH}Ph + Cl^- \quad (2e)$$

In an attempt to establish the details, we have examined how the kinetics and products are affected by change in structure, including substitution of deuterium for hydrogen in the side-chain.

[1] Soderbaum and Widman, *Ber.*, 1892, **25**, 3291.
[2] Walden and Kernbaum, *Ber.*, 1890, **23**, 1959.
[3] Bergmann and Hervey, *Ber.*, 1929, **62**, 893.
[4] Hahn, *Ber.*, 1929, **62**, 2485.
[5] Kleucker, *Ber.*, 1929, **62**, 2587.

Experimental

Benzyl chloride (b. p. 66—67°/16 mm.), 3-nitrobenzyl chloride (m. p. 45·5°), *p*-nitrobenzyl chloride (m. p. 72·5°), 2-nitrobenzyl chloride (m. p. 49·5°), 2,4-dinitrobenzyl chloride (m. p. 34°), *p*-nitrobenzaldehyde (m. p. 106·5°), *p*-methoxybenzaldehyde (b. p. 112°/10 mm.), *trans*-4,4′-dinitrostilbene (m. p. 288°), 4,4′-dinitrostilbene oxide (m. p. 200—201°), 2,4,2′4′-tetranitrostilbene (m. p. 260°), 2,4,4′-trinitrostilbene oxide (m. p. 142°) and 2,4,4′-trinitrostilbene (m. p. 235°) were prepared by standard methods and carefully purified. The solvents, after purification, had b. p.s within 0·1° and were always freshly prepared. An x% solution of acetone or dioxan was made by mixing x volumes of the organic solvent with $(100 - x)$ volumes of the acid or alkali solution just before the kinetic experiment.

α-Deutero-4-nitrobenzyl Chloride.—Side-chain chlorination of deuterated toluene [6] by Kharasch and Brown's method [7] gave α-deuterobenzyl chloride which on nitration [8] gave α-deutero-4-nitrobenzyl chloride. This was expected statistically to contain 33% of the non-deuterated material. On treatment with alkali in 50% dioxan, it gave αα′-dideutero-4,4′-dinitrostilbene (expected statistically to be only 33% deuterated). Comparison of the infrared spectra of deuterated and non-deuterated materials showed the presence of the following new absorption bands in the deuterated materials which must be attributed to the presence of the α-CD bond: *p*-$O_2N{\cdot}C_6H_4{\cdot}CHDCl$, 7·7w, 8·3w, 11·0s, 12·7vs, and 13·25s μ;

$$O_2N{\cdot}C_6H_4{\cdot}CD{:}CD{\cdot}C_6H_4{\cdot}NO_2 \text{ or } O_2N{\cdot}C_6H_4{\cdot}CD{:}CH{\cdot}C_6H_4{\cdot}NO_2,$$

10·95s and 12·95m μ.

Kinetic Measurements.—The rates of reaction were determined by following the rate of liberation of chloride by electrometric titration of aliquot parts of the mixture.[9] Most of the experiments were carried out in duplicate. It was shown that none of the organic materials interfered with the measurements. The following is an example of a typical kinetic run, with 4-nitrobenzyl chloride (0·01M) and sodium hydroxide (0·10M) in 50% aqueous dioxan at 30°:

Time (min.)	15·05	25·13	38·33	52·63	75·30	110·30	136·00
Reaction (%)	14·05	20·94	29·60	38·00	51·50	65·90	75·50
10^4k_1 (min.$^{-1}$)	101·0	93·5	94·5	94·6	96·0	96·2	103·2

The following are results for benzyl chloride (0·01M) in 50% aqueous dioxan:

Temp.	30	30	30	35	40
OH^- (M)	0·10	0·15	0·20	0·20	0·20
10^4k_1 (min.$^{-1}$)	2·8	4·0	5·25	10·6	18·0

Activation energy = 23,500 cal./mole.

Corresponding results for 4-nitrobenzyl chloride are:

Temp.	20	23	30	30	30	30	30
ArCl (M)	0·01	0·01	0·01	0·01	0·01	0·05	0·05
OH^- (M)	0·10	0·10	0·10	0·01	0·02	0·05	0·05
10^4k_1 (min.$^{-1}$)	38·7	50·7	96·8	—	—	—	—
10^4k_2 (l. mole^{-1} sec.$^{-1}$)	—	—	—	16·9	15·2	16·0	22·7 *

* In 70% dioxan.

Activation energy = 16,300 cal./mole.

Added *p*-methoxybenzaldehyde had little effect on the rate. Catalysis by added *p*-nitrobenzaldehyde is shown by the following two tables. Table 1 shows the percentages of reaction of 0·05M-4-nitrobenzyl chloride with 0·05M-sodium hydroxide (*a*) in the absence and (*b*) in the presence of 0·05M-*p*-nitrobenzaldehyde at 30° in 50% dioxan. Similarly, Table 2 shows the percentages of reaction between 0·01M-*p*-nitrobenzyl chloride and 0·1M-sodium hydroxide (*a*) in the absence and (*b*) in the presence of 0·01M-*p*-nitrobenzaldehyde at 30° in 50% dioxan.

For reactions in 50% dioxan at 30°, with 0·01M-ArCl and 0·1M-NaOH, the following values of k_1 were obtained: 2-nitrobenzyl chloride, $13·2 \times 10^{-4}$; 3-nitrobenzyl chloride, $4·35 \times 10^{-4}$.

[6] Turkevich, McKenzie, Friedman, and Spurr, *J. Amer. Chem. Soc.*, 1949, **71**, 4045.
[7] Kharasch and Brown, *J. Amer. Chem. Soc.*, 1939, **61**, 2147.
[8] Alway, *J. Amer. Chem. Soc.*, 1902, **24**, 1062.
[9] Best, *J. Agric. Sci.*, 1929, **19**, 533; Snyder, *Soil Sci.*, 1933, **35**, 43; Janz and Taniguichi, *Chem. Rev.*, 1953, **53**, 397; MacInnes and Beattie, *J. Amer. Chem. Soc.*, 1920, **42**, 1117; Smith, *J. Res. Nat. Bur. Standards*, 1929, **2**, 1137; Hine and Lee, *J. Amer. Chem. Soc.*, 1951, **73**, 22.

The reaction of 0·01M-2,4-dinitrobenzyl chloride with 0·01M-NaOH in 50% dioxan at 20° was 95% complete after 1 min.

TABLE 1.

Time (min.)		20	30	60	61	110	150	170	210	270
Reaction (%)	(*a*)	—	12·8	21·8	—	34·8	42·4	—	50·0	56·3
	(*b*)	17·6	—	—	34·7	45·5	—	52·7	55·8	—

TABLE 2.

Time (min.)		5	15	15·05	25·0	25·13	35	38·33	75·30
Reaction (%)	(*a*)	—	—	14·05	—	20·94	—	29·60	51·50
	(*b*)	20·5	50·3	—	66·5	—	76·0	—	—

Tracer Experiments.—4-Nitrobenzyl chloride (0·04M) and sodium hydroxide (0·04M) in dioxan–deuterium oxide (99·8%) (4 : 1 v/v) at 30° were allowed to react for 100 min.; about 38% of the chloride should have reacted. The unhydrolysed chloride was recovered; its infrared spectrum was determined and compared with that of the prepared sample, which is considered to be 66% deuterated. From the ratios of the heights of the absorption bands at 12·7 and at 6·1 μ, it can be calculated that the product is 42% deuterated. The infrared spectrum of 4,4′-dinitrostilbene isolated from the reaction showed the deuterium bands at 10·9 and 12·9 μ.

Deuterated 4-nitrobenzyl chloride (0·01M; 66% deuterium in the side-chain) reacted with alkali (0·1M) in 50% aqueous dioxan at 30° at a rate ($k_1 = 75 \times 10^{-4}$ min.$^{-1}$) slower by a factor of 1·28 than that (90×10^{-4} min.$^{-1}$) observed under the same conditions for the undeuterated material.

Reaction in Aqueous Acetone.—The following is a summary of kinetic measurements in aqueous acetone:

Benzyl chloride (0·013M), NaOH (0·13M), at 30° in 50% acetone, $k_1 = 3{\cdot}1 \times 10^{-4}$ min.$^{-1}$.

4-Nitrobenzyl chloride at 30°:

	ArCl (M)	OH^- (M)	10^4k_1 (min.$^{-1}$)	10^4k_2 (l. mole^{-1} sec.$^{-1}$)
In 50% acetone	0·01	0·10	191	—
	0·05	0·05	—	32·4
In 70% acetone	0·05	0·05	—	69·0

Products.—Under the conditions of the kinetic investigation, 4-nitrobenzyl chloride (0·01—0·05M) with alkali (0·01—0·1M) in aqueous ethanol, acetone, or dioxan gave almost quantitatively 4,4′-dinitrostilbene (*trans*-isomer, m. p. 288°; a little of the *cis*-isomer, m. p. 185°, was obtained from the mother-liquors).

The product was unchanged when the reaction was carried out in the presence of 4-nitrobenzyl alcohol or *p*-methoxybenzaldehyde. When it was carried out in the presence of *p*-nitrobenzaldehyde, 4,4′-dinitrostilbene oxide (m. p. and mixed m. p. 200—201°) was isolated.

2,4-Dinitrobenzyl chloride similarly gave 2,4,2′,4′-tetranitrostilbene, m. p. and mixed m. p. 260°, and, in the presence of *p*-nitrobenzaldehyde and anhydrous potassium carbonate in methanol gave the corresponding stilbene oxide, m. p. 142°, which with potassium iodide in glacial acetic acid gave 2,4,4′-trinitrostilbene, m. p. and mixed m. p. 235°.

DISCUSSION

The results show that the reaction of benzyl and of 4-nitrobenzyl chloride in the presence of alkali is of the second order:

$$d[Cl^-]/dt = k_2[ArCl][OH^-]$$

4-Nitrobenzyl chloride reacts faster (60 times in acetone, and 35 times in dioxan) than benzyl chloride. Such a result would not be expected if both compounds reacted by S_N2 displacement of halide; for the results of Olivier [10] and of Simonetta and Favini [11] show that, in such solvents, quite powerfully electron-withdrawing groups have little effect on the rate of the reaction. Thus the following relative rates were obtained for

[10] Olivier, *Rec. Trav. chim.*, 1930, **49**, 697, 996.
[11] Simonetta and Favini, *J.*, 1954, 1480.

substituted benzyl chlorides (p-R·C_6H_4·CH_2Cl; 0·01M) and hydroxide ion at 30·4° in 50% aqueous acetone: [12]

R	Me	H	CN		Me	H	CN
Rel. rate ($OH^- = 0·05M$)...	2·2	1	1·3	($OH^- = 0·10M$).....	3·2	1·8	2·5

The S_N2 mechanism dominates the reaction where R = CN or H, but much less where R = Me. The considerable reactivity of 4-nitrobenzyl chloride suggests that the first stage in its reaction with alkali is removal of a proton, which is shown to be reversible since 4-nitrobenzyl chloride recovered after partial reaction in dioxan–D_2O contains deuterium. Stage 2a of Hahn's mechanism is therefore not rate-determining; nor is stage 2b, since this would require that the reaction have the kinetic form $d[Cl^-]/dt = k[ArCl]^2[OH^-]$. The following modification, designated α-*ElcB*, is therefore suggested:

$$O_2N{\cdot}C_6H_4{\cdot}CH_2Cl + OH^- \rightleftharpoons O_2N{\cdot}C_6H_4{\cdot}CHCl^- + H_2O \quad . \quad . \quad . \quad . \quad . \quad (3a)$$

$$O_2N{\cdot}C_6H_4{\cdot}CHCl^- \xrightarrow{\text{Slow}} O_2N{\cdot}C_6H_4{\cdot}CH{:} + Cl^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (3b)$$

$$2O_2N{\cdot}C_6H_4{\cdot}CH{:} \longrightarrow O_2N{\cdot}C_6H_4{\cdot}CH{:}CH{\cdot}C_6H_4{\cdot}NO_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (3c)$$

Since p-nitrobenzaldehyde diverts the reaction to form an epoxide, with increase in the rate of liberation of chloride ion (the rate does not change in presence of the less reactive p-methoxybenzaldehyde and the product is the dinitrostilbene and not an epoxide), it is suggested that this process involves reaction between the intermediate ion $O_2N{\cdot}C_6H_4{\cdot}CHCl^-$ and the aldehyde, thus:

$$O_2N{\cdot}C_6H_4{\cdot}CHCl^- + O_2N{\cdot}C_6H_4{\cdot}CHO \xrightarrow[\text{Faster than (3}b\text{)}]{\text{Slower than (3}a\text{)}} O_2N{\cdot}C_6H_4{\cdot}\underset{\displaystyle Cl}{\overset{\displaystyle O^-}{\underset{|}{\overset{|}{C}}}}H{\cdot}CH{\cdot}C_6H_4{\cdot}NO_2$$

$$\xrightarrow{\text{Fast}} O_2N{\cdot}C_6H_4{\cdot}\underset{\displaystyle O}{\overset{\displaystyle /\!\backslash}{CH{-}\!-\!CH}}{\cdot}C_6H_4{\cdot}NO_2 + Cl^- \quad . \quad (3d)$$

This mechanism differs from Bergmann and Hervey's [3] in that it is considered that it is not the biradical but the conjugate base which reacts with the intercepting aldehyde.

If the rates of the forward and the backward reaction of (3a) are about the same and much greater than that of (3b), then α-deutero-4-nitrobenzyl chloride would be substantially converted into 4-nitrobenzyl chloride before hydrolysis by alkali in aqueous dioxan, and no deuterium isotope effect could be observed. The observation of a small effect (k_H/k_D = 1·28) suggests, therefore, that the *back-reaction* of (3a) is of a rate similar to that of (3b). The rate of the backward reaction (3a) is the same for both the deuterated and the non-deuterated material, since the same anion is formed by deuterium-extraction. Similarly, the rate of reaction (3b) is the same for both materials. The only variable is that of the forward reaction (3a), a proton- or a deuterium-extraction. The equilibrium constant (K_e) for (3a) will therefore vary according to whether the material is deuterated or not. The overall rate constant of the reaction [K_e × rate constant of the slow (3b) step] will consequently vary.

In the reaction of 2,4-dinitrobenzyl chloride, the overall rate of the reaction is much greater; the intermediate conjugate base must have been formed very easily under the influence of the two nitro-groups, and is clearly very reactive, readily losing halide ion or reacting with added aldehyde to form epoxide.

We are indebted to Professor D. H. Hey, F.R.S., and his colleagues for facilities provided at King's College, London, in 1956, and for helpful advice, to Dr. Shang Shih for determining the infrared spectra, and Professor P. B. D. de la Mare for his interest and suggestions with respect to the preparation of the manuscript.

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[12] Olivier and Weber, *Rec. Trav. chim.*, 1934, **53**, 869, 891.

40. *The Influence of the Nitro-group upon Side-chain Reactivity. Part II.*[1] *The Inhibition of the Influence of the Nitro-group upon α-Proton-extraction from 4-Nitrobenzyl Chloride.*

By Samir B. Hanna, Youssef Iskander, and (in part) Adib Salama.

The rates of liberation of chloride ion from 3-hydroxy- and 3-methoxy-4-nitrobenzyl chloride have been measured in initially neutral and in alkaline aqueous acetone and aqueous dioxan. In alkaline media, the formation of derivatives of 4,4′-dinitrostilbene was inhibited by the presence of the O^- substituent *ortho* to the nitro-group, and the rate of reaction was similar to that of the alkaline hydrolysis of benzyl chloride. An *o*-methoxyl group was less effective. It is suggested that the electron-withdrawing power of the nitro-group is reduced by mesomeric interaction with adjacent OMe and especially O^- substituents.

The nitro-group has been shown [1] to promote the formation of the appropriate derivative of stilbene from *p*-nitrobenzyl chloride in its reaction with nucleophilic reagents. In the present work, the influence of methoxyl and hydroxyl groups *ortho* to the nitro-group has been examined in acid and in alkaline media, to determine whether the methoxyl, hydroxyl, and O^- substituents modify the activating power of the nitro-group for this reaction.

Experimental

3-Hydroxy-4-nitrobenzyl alcohol, m. p. 97° (lit.,[2] 97°), was prepared from 3-hydroxy-4-nitrobenzaldehyde by reduction with isopropyl alcohol and aluminium isopropoxide. *3-Hydroxy-4-nitrobenzyl chloride* was prepared from the alcohol (3 g.) in benzene (30 ml.), phosphorus pentachloride (3·7 g.) being added in small portions with constant shaking. The mixture was warmed for a few minutes, then cooled and poured into ice-cold water. The benzene layer contained a viscous residue which crystallised from light petroleum in yellow needles, m. p. 48° (2 g.) (Found: C, 44·9; H, 3·2; N, 8·0; Cl, 18·9. $C_7H_6ClNO_3$ requires C, 44·8; H, 3·2; N, 7·5; Cl, 18·9%).

3-Methoxy-4-nitrobenzyl alcohol, prepared similarly, crystallised from benzene–light petroleum in colourless needles, m. p. 96° (Found: C, 52·9; H, 4·9; N, 7·7. $C_8H_9O_4N$ requires C, 52·5; H, 4·9; N, 7·7%). It was converted by phosphorus pentachloride into the *chloride* that crystallised from light petroleum in colourless needles, m. p. 68° (Found: C, 47·6; H, 4·1; N, 6·9; Cl, 17·6. $C_8H_9O_3NCl$ requires C, 47·6; H, 4·0; N, 6·9; Cl, 17·6%).

Kinetics.—The reactions in alkaline media were followed as described in the previous paper. The reactions in initially neutral solution were very slow at 30°; measurements were made for runs at 60° in sealed ampoules. Most of the experiments were carried out in duplicate. The following is an example of a typical kinetic run, for 3-methoxybenzyl chloride (0·01M) and OH^- (0·10M) in 50% dioxan at 30°:

Time (hr.)	10	25	40	50	60	75
Reaction (%)	14·9	33·9	48·8	55·8	62·5	70·4
10^4k_1 (min.$^{-1}$)	2·69	2·77	2·78	2·73	2·74	2·71

The annexed Table summarises the results.

Rates of reaction of 3-substituted 4-nitrobenzyl chlorides, initially 0·01M.

3-Subst.	Temp.	Solvent	OH^- (M init.)	10^4k_1 (min.$^{-1}$)	3-Subst.	Temp.	Solvent	OH^- (M init.)	10^4k_1 (min.$^{-1}$)
H	30°	50% dioxan	0·10	96·8 [a]	OH	40°	50% dioxan	0·21	9·72 [b]
OH	30	50% dioxan	0·11	1·70	OMe ...	30	50% dioxan	0·10	6·4
OH	30	50% acetone	0·11	1·99					(rising)
OH	30	50% dioxan	0·21	3·12 [b]	OH	60	50% acetone	0·00	0·35
					OMe ...	60	50% acetone	0·00	0·51

[a] Ref. 1. [b] Activation energy calc. 21,700 cal./mole.

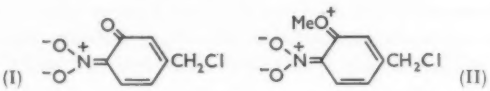
[1] Part I, preceding paper.
[2] Lock, *Ber.*, 1929, **62**, 1184.

XUM

The product from the reaction of 3-hydroxy-4-nitrobenzyl chloride with alkali was shown to be the alcohol; 3-methoxy-4-nitrobenzyl chloride did not give the alcohol; it gave material, m. p. 150° (Found: C, 55·5; H, 4·0; N, 8·0%), probably the impure stilbene; in this experiment, the integrated rate coefficients, k_1, determined through the course of the reaction, rose from $6{\cdot}4 \times 10^{-4}$ min.$^{-1}$ at 5·5% reaction to $12{\cdot}0 \times 10^{-4}$ at 67·5% reaction.

Discussion

It was shown in the previous paper that reaction of 4-nitrobenzyl chloride with alkali in aqueous acetone or aqueous dioxan is very much more rapid than of benzyl chloride and gives the stilbene. The similar reaction of 3-hydroxy-4-nitrobenzyl chloride has a rate similar to that of benzyl or 3-methoxybenzyl chloride and gives the alcohol. The activation energies bear the expected relationship. Under these experimental conditions, the hydroxyl group must be converted into O^-; it is clear that the negatively charged oxygen atom *ortho* to the nitro-group has prevented extraction of a proton from the CH_2Cl group, so that the reaction no longer gives a stilbene derivative. It is suggested that the O^- substituent prevents the nitro-group from exerting its strong electron-withdrawing influence by mesomerism involving structure (I):



For 3-methoxy-4-nitrobenzyl chloride, reaction is complicated and does not lead to a simple kinetic equation; perhaps hydrolysis and α-proton-extraction occur side by side at different rates. The initial rate of reaction is, however, notably more rapid than that of benzyl chloride, but much less than that of 4-nitrobenzyl chloride; probably some resonance interaction (structure II) reduces the effectiveness of the nitro-group and diminishes the relay of electrons from the side-chain.

The following are the rate coefficients for hydrolyses of substituted benzyl halides (0·01M) in 50% aqueous acetone at 60°, the solutions being initially neutral:

CH_2PhCl deriv.	Unsubst.	4-NO_2	3-HO-4-NO_2	3-MeOH-4-NO_2
10^5k_1 (min.$^{-1}$)	46	4·6	3·6	5·1

The hydrolysis of benzyl chlorides in neutral medium usually proceeds by the S_N1 mechanism.[3] The *p*-nitro-group, attached alone to the nucleus, reduces the rate considerably (from 46×10^{-5} to $4{\cdot}6 \times 10^{-5}$ min.$^{-1}$), by its $-T$ and $-I$ effects. The influence of *m*-hydroxyl or *m*-methoxyl on the electron-attracting influence of the *p*-nitro-group, although very slight, yet seems to be observable. The *m*-hydroxyl reduced the rate still further to $3{\cdot}6 \times 10^{-5}$ min.$^{-1}$ (contributing with its $-I$ effect; probably also the hydrogen bonding between OH and NO_2 has caused coplanarity of the NO_2 with the ring, thus increasing its attraction of electrons from the side-chain). *m*-Methoxyl, on the other hand, increased the rate slightly (to $5{\cdot}1 \times 10^{-5}$ min.$^{-1}$): it should have contributed also with its $-I$ effect (no hydrogen bonding in this case). Therefore the slight increase in the rate may be due to interaction between the NO_2 and the OMe group, which has counterbalanced the $-I$ effect and also decreased to a slight extent the attraction of electrons from the side-chain.

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[3] Olivier, *Rec. Trav. chim.*, 1922, **41**, 646; 1923, **42**, 775.

41. *Carbon–Sulphur Fission in Thioethers. Part IV.*[1] *The Mechanism of Base-catalysed Elimination from 4-Nitrophenethylthio-derivatives of Acetic, Propionic, and Related Acids.*

By Youssef Iskander and Youssef Riad.

The action of dilute alkali on acids $O_2N{\cdot}C_6H_4{\cdot}CH_2{\cdot}CH_2{\cdot}SZ$ gives 4-nitrostyrene in amounts varying according to the nature of Z and the concentration of alkali. At higher concentrations of alkali (8 equiv., 1·25M) the α-proton-extraction was much faster than elimination of SZ^- from the conjugate base, and accordingly brown-red acids containing nitrogen and sulphur became the main products. Increase in the electronegativity of the sulphur by the introduction of phenyl groups into Z resulted in complete, probably *E*2, elimination, unaccompanied by the formation of brown-red acids. Partial reversibility of the first stage was confirmed in one example by showing that deuterium in the solvent became incorporated in the starting material recovered after partial reaction.

Eliminations, having second-order kinetics, generally have the *E*2 mechanism. The *ElcB* mechanism predicted by Skell and Hauser[2] and discussed by Ingold[3] has been sought by examining reaction in a deuterated solvent and determining deuterium in the starting material recovered after partial reaction. This method, applied to phenethyl bromide, showed no evidence for incorporation of deuterium.

In acids of the type $O_2N{\cdot}C_6H_4{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}CRR'{\cdot}CO_2H$, the *p*-nitro-group is expected to facilitate proton-removal from the α-CH_2 group, and the $S{\cdot}CRR'{\cdot}CO_2H$ substituent should be liberated as an anion much less readily than is, for example, the bromide ion from $p\text{-}O_2N{\cdot}C_6H_4{\cdot}\bar{C}H{\cdot}CH_2Br$. The action of bases on these compounds has therefore been examined, to see whether this system is suitable for observation of the *ElcB* mechanism (equations 1, 2 with $v_{-1} > v_2$) (cf. ref. 4):

$$OH^- + O_2N{\cdot}C_6H_4{\cdot}CH_2{\cdot}CH_2{\cdot}S{\cdot}CRR'{\cdot}CO_2^- \underset{v_{-1}}{\overset{v_1}{\rightleftharpoons}} O_2N{\cdot}C_6H_4{\cdot}\bar{C}H{\cdot}CH_2{\cdot}S{\cdot}CRR'{\cdot}CO_2^- + H_2O \quad . \quad (1)$$

$$O_2N{\cdot}C_6H_4{\cdot}\bar{C}H{\cdot}CH_2{\cdot}S{\cdot}CRR'{\cdot}CO_2^- \xrightarrow{v_2} O_2N{\cdot}C_6H_4{\cdot}CH{:}CH_2 + {}^-S{\cdot}CRR'{\cdot}CO_2^- \quad . \quad . \quad . \quad . \quad (2)$$

Experimental

β-4-*Nitrophenethylthiopropionic Acid.*—4-Nitrophenethyl chloride (5 g.) in alcohol (70 ml.) was treated with a solution of β-mercaptopropionic acid (2·9 g.) and sodium hydrogen carbonate (4·8 g.) in water (20 ml.). The mixture was boiled for 1 hr., cooled, and diluted with water. After removal of turbidity by extraction with ether, acidification gave the *acid* (5·7 g.), m. p. 63—65° (from benzene–light petroleum) (Found: C, 51·6; H, 4·8; N, 5·3; S, 12·9. $C_{11}H_{13}NO_4S$ requires C, 51·8; H, 5·1; N, 5·5; S, 12·5%).

A neutral aqueous solution of the acid, after being boiled for 1 hr., gave only a slight odour of 4-nitrostyrene. In the presence of a slight excess of sodium hydrogen carbonate the same result was obtained. Acidification in these experiments liberated the original acid.

Action of alkalis. (*a*) The acid (2 g.) was boiled in 5% aqueous sodium hydroxide (50 ml., *ca.* 8 equiv.) for 5 min. Steam-distillation of the deep red solution gave 4-nitrostyrene.[1] Acidification of the alkaline residue gave a brown-red acid (0·64 g.) which on purification by repeated precipitation from sodium hydrogen carbonate solution was obtained as a brown-red infusible powder (Found: C, 59·9; H, 4·5; N, 6·5; S, 9·5%). (*b*) When 1—3 equiv. of alkali were used, some 4-nitrostyrene was formed, but on acidification the residue of the original acid was recovered unchanged.

[1] Part III, *J.*, 1951, 2058.
[2] Skell and Hauser, *J. Amer. Chem. Soc.*, 1945, **67**, 1661.
[3] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, p. 423.
[4] Hanna, Iskander, and (in part) Riad, *J.*, 1961, 217.

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α-4-*Nitrophenethylthiopropionic Acid*.—This was prepared similarly from α-mercaptopropionic acid, and had m. p. 85—86° (from benzene–light petroleum) (Found: C, 51·7; H, 4·9; N, 5·4; S, 12·2%). The *acid*, on being boiled with dilute alkali (1—3 equiv.), gave 4-nitrostyrene and unchanged starting material. On being boiled with 5% alkali (8 equiv.) it gave 4-nitrostyrene and a brown-red acid (0·65 g.) (Found: C, 56·8; H, 4·7; N, 6·3; S, 8·1%).

α-*Methyl*-α-(4-*nitrophenethylthio*)*propionic Acid*.—Prepared similarly, this *acid* had m. p. 103—104° (from benzene–light petroleum) (Found: C, 53·8; H, 5·5; N, 5·6; S, 11·2. $C_{12}H_{15}NO_4S$ requires C, 53·5; H, 5·6; N, 5·2; S, 11·9%). When boiled with dilute alkali (1—3 equiv.) it gave *p*-nitrostyrene and unchanged starting material; and with 5% alkali (8 equiv.) it gave 4-nitrostyrene and a brown-red acid (Found: C, 57·1; H, 4·8; N, 5·9; S, 9·4%).

α-4-*Nitrophenethylthio*-αα-*diphenylacetic Acid*.—Prepared similarly from 4-nitrophenethyl chloride and α-mercaptodiphenylacetic acid, this *acid* had m. p. 192° (from ethanol) (Found: C, 67·2; H, 4·9; N, 3·0; S, 7·5. $C_{22}H_{19}NO_4S$ requires C, 67·2; H, 4·8; N, 3·6; S, 8·1%). When it (2·0 g.) was boiled with 5% sodium hydroxide solution (50 ml.) for 5 min., the solution became pale red and on steam-distillation gave 4-nitrostyrene; the alkaline residue gave α-mercaptodiphenylacetic acid.

Estimation of 4-*Nitrostyrene*.—Absolute determination of 4-nitrostyrene could not be carried out, but the following approximate method gave consistent results which established trends in the amount formed in the different experiments. The following is an example. β-4-Nitrophenethylthiopropionic acid (0·20 g.) was dissolved in 0·340N-sodium hydroxide (2·3 ml., one equiv.), made up to 50 ml. with water, and brought to the b. p. in exactly 5 min. Boiling was continued for a further 30 min. The solution was cooled for 2 min., then distilled at a rate of about 1·25 ml./min., so as to collect 30 ml., distilled water being added during this process from a separating funnel so that the volume in the distilling flask remained nearly constant. The whole process took 62·5 min. To the distillate (30 ml.) was added purified acetone (30 ml.) and 2N-sulphuric acid (60 ml.), and the mixture was titrated immediately with 0·1164N-potassium permanganate at laboratory temperature until a faint pink colour persisted for 30 sec. The experiment was repeated with 3·45, 4·60, and 6·90 ml. of the alkali (1·5, 2, and 3 equiv. respectively).

The annexed Table shows the detailed results.

Formation of 4-*nitrostyrene from acids* $O_2N{\cdot}C_6H_4{\cdot}CH_2{\cdot}CH_2{\cdot}SZ$.

Group Z	Starting material (g.)	Oxidisable product formed (expressed in ml. of 0·1164N-$KMnO_4$) NaOH 1·0 equiv.	NaOH 1·5 equiv.	NaOH 2·0 equiv.	NaOH 3·0 equiv.
$CH_2{\cdot}CO_2H$	0·1890	0·18	1·95	3·24	5·48
$CHMe{\cdot}CO_2H$	0·2000	0·12	1·70	3·14	5·18
$CMe_2{\cdot}CO_2H$	0·2109	0·07	1·30	2·80	4·14
$CH_2{\cdot}CH_2{\cdot}CO_2H$	0·2000	0·27	1·65	2·47	4·18
$CPh_2{\cdot}CO_2H$	0·3082	0·37	1·88	2·94	4·86

Reaction in Deuterium Oxide.—α-4-Nitrophenethylthioacetic acid [1] (0·11 g.) was dissolved in 99·5% deuterium oxide (10 ml.) containing sodium hydroxide (0·0365 g., 2 equiv.). The mixture was boiled for 1 hr., cooled, and acidified. Some unchanged acid was liberated; crystallised from aqueous ethanol, this had m. p. 85°. Comparison of the infrared spectrum of the recovered acid with that of the original sample showed the presence of new bands, as well as the shift of others to longer wavelengths. Attempts to prepare a synthetic sample of the deuterated acid of known deuterium content failed (see below), but other related compounds were prepared and investigated for comparison. Starting from [α-^{2}H]toluene gave the compounds shown in the Table by standard methods. The chlorination, (*a*)→(*b*), is assumed to give a product containing 66% of deuterium in the side-chain, and accordingly compounds (*e*), (*f*), and (*g*) are considered to have the same percentage of side-chain deuterium. Acid-hydrolysis of the nitriles (*f*) and (*g*), and reduction of the nitrile (*f*) by sodium and ethanol, followed by nitration of the resulting amine to obtain 4-nitrophenethylamine hydrochloride (*i*), gave products having infrared spectra identical with those of the appropriate undeuterated materials. So hydrogen–deuterium exchange, probably activated by the cyano-group, must have occurred during the reduction or the hydrolysis of the nitriles.

The Table summarises the important clear changes in infrared spectra [5] [determined in Nujol, except that (*d*) and (*f*) were examined in CCl_4]. New bands and band shifts appearing for the acid (*h*) (recovered from the reaction mixture described above after partial reaction) are present also in the spectra of other α-deuterated compounds; the band at 7·7 μ, which is the clearest new one in this spectrum, is present also in the spectra of compounds (*a*), (*d*), (*e*), and (*f*). Similarly the shift from 12·6 to *ca.* 12·9 μ is probably attributable to a band at 12·7 μ in the spectrum of compound (*e*), and may also be responsible for the increased strength of the similar band for (*a*) and for the shifts with (*b*) and (*c*). The band at 13·5 μ for the acid (*h*) is found in a similar region for compounds (*a*) and (*e*), and might have caused the shifts for compounds (*b*) and (*c*). It is concluded that compound (*h*) contained deuterium incorporated in the α-position to the phenyl group.

Infrared absorption bands and spectral changes attributable to C–D *bonds α to a phenyl group.*

Compound	Wavelength (μ)						
$Ph{\cdot}CH_2D$ (*a*)	4·45		7·7		9·25infl 9·65infl	12·65infl	13·8
$p\text{-}O_2N{\cdot}C_6H_4{\cdot}CH_2D$ (*b*)						12·65 →	13·5 →
						12·85	13·6
$2,4\text{-}(O_2N)_2C_6H_3{\cdot}CH_2D$ (*c*)						12·60 →	13·0 →
						12·80	13·2
$Ph{\cdot}CHDCl$ (*d*)	4·4, 4·6w	5·7	7·7sh	8·3infl		11·1	
$p\text{-}O_2N{\cdot}C_6H_4{\cdot}CHDCl$ (cf. 3) (*e*)			7·7w	8·3w		11·0 12·7	13·25
$Ph{\cdot}CHD{\cdot}CN$ (*f*)	4·7w	5·8	7·85				
$p\text{-}O_2N{\cdot}C_6H_4{\cdot}CHD{\cdot}CN$ (*g*)		5·97w		8·25w	10·25w	11·15w	
$p\text{-}O_2N{\cdot}C_6H_4{\cdot}CHD{\cdot}CH_2{\cdot}S{\cdot}CH_2CO_2H$ (*h*)			7·7		9·55	12·6 → 12·95	13·5

infl = Original band at same wavelength greatly increased in strength; → = Band shifted to slightly longer wavelength; sh = shoulder on the 7·9 μ band; w = weak new band.

It may be noted that the new band at 4·4—4·7 μ, found in the spectra of compounds (*a*), (*d*), and (*f*) which do not contain a nitro-group, is absent from the spectra of the corresponding nitro-compounds.

Discussion

For all the acids investigated, the rate of the elimination was increased by increase in the concentration of alkali up to about 3 equiv. Further increase in the concentration of alkali (to about 8 equiv.) introduced a side reaction involving partial transformation of the acids into resinous brown-red acids containing nitrogen and sulphur in the atomic ratio *ca.* 3 : 2. If the second stage of the reaction (v_2, reaction 2) were faster than the first (v_1, reaction 1), then all the carbanions would have reacted to form the corresponding derivative of styrene, as soon as they had been formed. It is suggested that in the present example the first stage is the faster, and hence the accumulation of the conjugate base, caused by increasing the concentration of alkali, has given an opportunity for the side reaction to occur. The N : S ratio, *ca.* 3 : 2 for the brown-red acids, suggests that every two carbanions have united with one 4-nitrostyrene molecule to give a complex structure. This result was found in each case except for the compound $RS{\cdot}CPh_2{\cdot}CO_2H$ which gave no brown-red acid even at high concentration of alkali, but instead 4-nitrostyrene and thiobenzilic acid. This means that the phenyl groups have increased the electron-attraction towards the sulphur atom, and accordingly the rate of the second stage has increased, leaving no chance for an accumulation of the conjugate base to form the brown-red acid; accordingly, for $RS{\cdot}CPh_2{\cdot}CO_2H$ the elimination seems to proceed by the *E*2 mechanism [reactions (1) and (2), with $v_2 \gg v_1$, $v_2 \gg v_{-1}$], and the case becomes similar to the decomposition of the quaternary ammonium salt $p\text{-}O_2N{\cdot}C_6H_4{\cdot}CH_2{\cdot}CH_2{\cdot}NMe_3^+$ to 4-nitrostyrene and trimethylamine.[6]

In all the other cases (cf. Table), the reaction probably proceeds by the *ElcB* mechanism;

[5] Cf. Turkevich, McKenzie, Friedman, and Spurr, *J. Amer. Chem. Soc.*, 1949, **71**, 4045.
[6] Hughes and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 659.

and it was proved that the first stage of the reaction is reversible (v_2 is much less than v_1 or v_{-1}) by establishing that deuterium from the solvent becomes incorporated in the starting material recovered after partial reaction of $RS{\cdot}CH_2{\cdot}CO_2H$ with dilute alkali.

The authors are grateful to the U.A.R. atomic energy establishment in Cairo for supplying the heavy water, and to Professor F. G. Baddar (A'in Shams University, Cairo) for the infrared curves determined in his laboratory. The authors acknowledge their indebtedness to Professor P. B. D. de la Mare, D.Sc., for his interest and suggestions with respect to the preparation of the manuscript.

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42. *Effect of Solvent Composition on the Kinetics of Reactions between Ions and Dipolar Molecules. Part III.*[1]

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A kinetic study of the exchange of radioactive iodine between sodium iodide and n-butyl iodide has been made in a series of mixtures of methyl cyanide and methanol as solvents, with carrier-free sodium radio-iodide providing all the iodide ions present initially. The reaction rate falls as the concentration of methanol is increased and this reduction in rate has been discussed in terms of a specific interaction between iodide ions and methanol molecules: changes in dielectric constant are small and have been neglected.

It has also been found, by the use of various phenols in place of methanol, that the capacity of a hydroxylic compound to retard the iodine exchange reaction increases with its strength as an acid. However, the integrated intensity of the infrared absorption band associated with the O–H stretching vibration appears to be a better measure than its acid strength of the capacity of a phenol to retard iodine exchange.

Spectroscopic evidence for hydrogen-bonding between anions and hydroxylic molecules is discussed briefly.

IN previous investigations into the effect of solvent composition on the kinetics of reactions between ions and dipolar molecules,[1,2] we have been concerned with the effect of water on the rate in acetone solution of reactions between iodide ions and n-butyl halides. Reductions in the rates of these reactions produced by progressively increasing the water concentration cannot be satisfactorily ascribed to changes in dielectric constant alone. We have, therefore, postulated the existence of two kinetically distinguishable ionic species, designated as I^- and $(I,H_2O)^-$, in the solution, the relative proportions of the two species being assumed to depend on the concentration of water present. Quantitative interpretation of experimental kinetic data in terms of this hypothesis was, of course, only possible after the rate constants obtained with various water concentrations had been corrected for differences in dielectric constant of the solvent. The method by which this correction was made was open to a number of objections, so that in the present investigation we have tried to avoid the need for such a correction by using mixtures of methyl cyanide ($\varepsilon = 35{\cdot}9$ at 30°) [3] and methanol ($\varepsilon = 31{\cdot}6$ at 30°) [3] as solvents in our kinetic experiments, methanol and water being expected to interact similarly with iodide ions.

Rate measurements on the isotopic exchange reaction $*I^- + Bu^nI \rightleftharpoons I^- + Bu^n*I$ have been made over the entire range of solvent compositions from pure methyl cyanide to pure methanol. Carrier-free sodium radio-iodide provided all the iodide ions present

[1] Part II, Cavell and Speed, *J.*, 1960, 1453.
[2] Cavell, *J.*, 1958, 4217.
[3] Simmonds, personal communication.

initially, so that rate constants did not require correction for ion association.[4] In most of our experiments, kinetic observations were confined to periods of less than 19 hr., *i.e.*, less than one-tenth half-life of ^{131}I. Eqn. (1), in which x is the radioactivity associated with n-butyl iodide at time t, c is the total radioactivity present, and a is the concentration of n-butyl iodide, was therefore used to obtain the rate constants k_2, which were usually evaluated graphically.

$$k_2 t = -(2{\cdot}303/a) \log_{10} (1 - x/c) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

In those experiments where k_2 was less than 10^{-4} l. mole^{-1} sec.$^{-1}$, measurements were necessarily made over longer periods than 19 hr. In such cases, the relevant rate constants were evaluated by means of eqn. (2), which allows for radioactive decay,[4] λ being the decay constant of ^{131}I, *viz.*, $1{\cdot}002 \times 10^{-6}$ sec.$^{-1}$. Rate constants k_2 calculated from kinetic

$$k_2(1 - e^{-\lambda t}) = -(2{\cdot}303\lambda/a) \log_{10} (1 - x/c) \quad . \quad . \quad . \quad . \quad (2)$$

measurements at three temperatures are summarised in Table 1.

TABLE 1. *Rate constants (k_2 in l. mole^{-1} sec.$^{-1}$) obtained with various mixtures of methanol and methyl cyanide as solvents.*

$[Bu^nI]_0 = 0{\cdot}030$—$0{\cdot}035$M.

Temp. = 19·71°.

[MeOH] (M)...	0	0	0·501	1·02	2·19	5·01	10·0	22·3	24·7 *
10^3k_2	1·85	2·00	1·40	0·972	0·570	0·219	0·103	0·0414	0·0358, 0·0363

Temp. = 32·50°

[MeOH] (M)...	0	0	0	0·246	0·501	0·790	1·02	2·19
10^3k_2	7·43	7·96	7·80	6·42	5·50	4·70	4·18	2·11
[MeOH] (M)...	3·28	5·01	10·0	17·0	22·0	24·3 *	24·3	24·3
10^3k_2	1·44	0·981	0·416	0·228	0·155	0·152	0·154	0·144

Temp. = 45·00°.

[MeOH] (M)...	0	0	0·501	1·02	2·19	5·01	16·7	21·6	24·0 *
10^3k_2	23·6	24·2	16·9	12·1	7·43	3·19	0·809	0·560	0·492

* Pure MeOH.

TABLE 2. *Variation of dielectric constant (ε) of mixtures of methanol and methyl cyanide with mol.-fraction of methanol (N) at 30·0°.*

N	0	0·127	0·244	0·398	0·562	0·663	0·790	0·916	1
ε	35·93	35·58	35·25	34·90	34·46	34·04	33·27	32·44	31·64

The progressive reduction in the specific rate constant of the iodine exchange reaction produced by increasing the proportion of methanol in the solvent is illustrated in Fig. 1, where log k_2 has been plotted against concentration of methanol. The variation of rate constant observed can hardly be attributed to changes in dielectric constant, since, as indicated in Table 2, this falls in value with increasing methanol concentration.[3] Theoretically, for reactions between ions and dipolar molecules, a reduction in dielectric constant would be expected to increase the rate constant. However, in the present investigation the overall change in dielectric constant is quite small, and such effect as is caused has been neglected altogether: the observed variation of rate constant with solvent composition is attributed entirely to an equilibrium $I^- + MeOH \rightleftharpoons (I,HOMe)^-$, the ions I^- and $(I,HOMe)^-$ being assumed to react with n-butyl iodide at different specific rates, namely, k_0 and k_∞ respectively. It follows from this equilibrium that the quotient $(k_0 - k_2)/[MeOH]$ should be directly proportional to the experimental rate constant k_2 appropriate to the methanol concentration chosen,[1] k_0 being the rate constant obtained with pure methyl cyanide.

In Fig. 2, $(k_0 - k_2)/[MeOH]$ has been plotted against k_2 for the experimental results obtained at 32·5° given in Table 1. Points corresponding to the lower concentrations

[4] Swart and le Roux, *J.*, 1956, 2110.

of methanol lie close to the same straight line in satisfactory agreement with the requirements of the equilibrium postulated above. However, deviations from this line are observed when the methanol concentration exceeds 1M. These are probably too large to be attributed to random experimental error and are in the wrong sense to be due to the failure to correct for the variation of dielectric constant.

There is the further possibility, especially at high concentrations of methanol, that significant errors in the values of k_2 might arise from neglect of the reaction between n-butyl iodide and the solvent methanol. Errors from side reactions of this kind may

FIG. 1. *Plot of* $(4 + \log_{10} k_2)$ *against concentration of methanol for data given in Table* 1 *for* 32·5°.

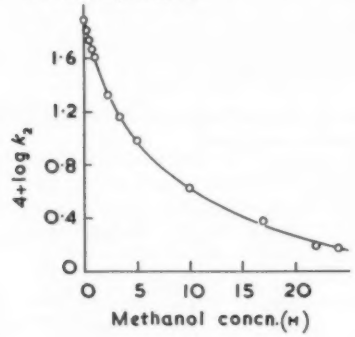
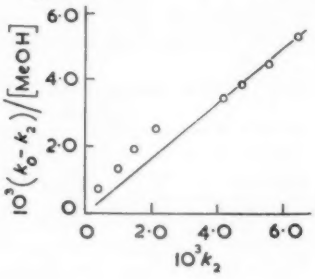


FIG. 2. *Plot of* $(k_0 - k_2)/[\text{MeOH}]$ *against* k_2 *for data given in Table* 1 *for* 32·5°.



be avoided, however, by the use of equation (3) to calculate the second-order rate constant k_2 of the exchange reaction,[4] k being the pseudo-first-order constant of the solvolysis, which is assumed to be irreversible; the other symbols have their previous significance.

$$k_2 t = -(2{\cdot}303/a) \log_{10} (1 - e^{-kt} x/c) \quad . \quad . \quad . \quad . \quad . \quad (3)$$

From measurements at 45° in pure methanol as solvent, we have found k to be about 2×10^{-8} sec.$^{-1}$. Errors in the value of k_2 arising from methanolysis of the alkyl halide are, therefore, negligible, since the factor e^{-kt} appearing in eqn. (3) will not be significantly less than unity until t reaches a value far in excess of 19 hr. At temperatures lower than 45°, methanolysis will probably be even less important because its energy of activation is likely to be larger than that of the iodine exchange reaction.

It seems, therefore, that the divergence from the straight line of points corresponding to higher concentrations of methanol, illustrated in Fig. 2, is probably not due to errors in the experimental rate constants. However, provided that the concentration of methanol does not exceed M, the variation of rate constant with solvent composition may be adequately accounted for in terms of the proposed equilibrium between iodide ions, methanol molecules, and the ionic species $(I,HOMe)^-$. It is possible, too, that the range of methanol concentrations over which this explanation satisfactorily accounts for the kinetic results might be extended by expressing methanol concentrations as thermodynamic activities.

The Arrhenius parameters of the iodine exchange reaction are shown in Table 3. They were calculated graphically from the rate constants given in Table 1. The pre-exponential

TABLE 3. *Parameters of the equation,* $k_2 = A_2 \exp(-E_A/RT)$ *(with* A_2 *in l. mole*$^{-1}$ *sec.*$^{-1}$*, and* E_A *in kcal. mole*$^{-1}$*), for rate constants given in Table* 1.

[MeOH] (M)	0	0·50	1·02	2·19	5·0	10·0	16·9	22·0	24·3
$\log_{10} A_2$	11·1	10·8	10·9	10·8	11·1	10·5	10·3	9·9	10·0
E_A	18·5	18·3	18·6	18·9	19·7	19·4	19·5	19·2	19·3

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factors A_2 tend to decrease in value as the proportion of methanol in the solvent is increased, although the overall change in log A_2 is quite small. The value of the energy of activation E_A, on the other hand, increases with increasing methanol concentration, reaching a maximum of 19·7 kcal. mole^{-1} at about 5M-methanol, above which concentration it remains almost constant.

In the interpretation of the effect of methanol upon the rate of the iodine exchange reaction discussed above, no assumptions about the nature of the interaction between iodide ion and hydroxylic molecule needed to be made. However, if this interaction involves the hydrogen atom of the hydroxyl group, then we should expect that the larger the acid dissociation constant K_a of the hydroxylic compound concerned, the larger would be the value of the association constant K_s for the equilibrium $I^- + ROH \rightleftharpoons (I,HOR)^-$. Thus if methanol were replaced by phenol in our kinetic experiments, we should expect the slope of the straight line obtained by plotting $(k_0 - k_2)/[ROH]$ against k_2 to be larger in the case of phenol, because the slopes of such plots are equal to the appropriate association constants.

So we measured the rate of the isotopic exchange reaction $*I^- + Bu^nI \rightleftharpoons I^- + Bu^n*I$ in methyl cyanide containing various concentrations, up to about M, either of phenol or of some *meta-* or *para*-substituted phenols covering a range of acid strengths. As in our experiments with methanol, carrier-free sodium radio-iodide provided all the iodide ions present initially, and rate constants were evaluated graphically by means of eqn. (1). These are recorded in Table 4.

TABLE 4. *Rate constants (k_2 in l. mole^{-1} sec.$^{-1}$) obtained with various phenols present in methyl cyanide as solvent.*

$[Bu^nI]_0$ = 0·030—0·035M. Temp. = 32·50°.

Phenol						
[ROH] (M)	0·251	0·382	0·499	0·501	0·797	0·997
10^3k_2	4·59	3·84	2·70	2·96	1·86	1·56
***p*-Methoxyphenol**						
[ROH] (M)	0·249	0·384	0·498	0·501	0·788	0·998
10^3k_2	4·56	3·54	2·54	2·94	1·95	1·60
***p*-Chlorophenol**						
[ROH] (M)	0·145	0·250	0·382	0·500		
10^3k_2	4·80	3·42	2·34	1·82		
***m*-Chlorophenol**						
[ROH] (M)	0·154	0·250	0·401	0·505		
10^3k_2	4·20	3·14	2·20	1·75		
***m*-Nitrophenol**						
[ROH] (M)	0·103	0·145	0·147	0·253	0·402	
10^3k_2	4·22	3·52	3·35	2·15	1·43	
***p*-Nitrophenol**						
[ROH] (M)	0·101	0·150	0·250	0·501		
10^3k_2	3·79	3·04	2·20	1·20		
2,4,6-Tribromophenol						
[ROH] (M)	0·150	0·250	0·401			
10^3k_2	6·90	6·48	5·90			

To illustrate the effect of increasing acid strength of the hydroxylic compound on the value of the association constant, we have, in Fig. 3, plotted $(k_0 - k_2)/[ROH]$ against k_2 for methanol and for each of the phenols studied. In most of the examples considered, the slope of the best straight line drawn through the experimental points increases as the acid strength of the hydroxylic compound increases. A complete comparison between association constants, evaluated graphically from plots shown in Fig. 3, and acid dissociation constants in water [5] of the phenols concerned is given in Table 5. There is evidently

[5] Judson and Kilpatrick, *J. Amer. Chem. Soc.*, 1949, **71**, 3110; Biggs, *Trans. Faraday Soc.*, 1956, **52**, 35.

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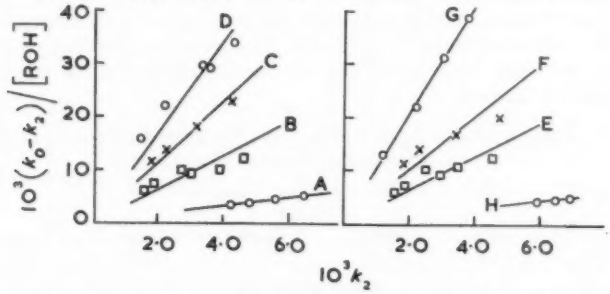
no simple quantitative relation between K_s and K_a and none would be expected. Nevertheless, it is generally true that, other things being equal, the capacity of a phenol to retard the iodine exchange reaction increases with its strength as an acid, a result which can be

TABLE 5. *Comparison of association constants (K_s) with acid dissociation constants in water (K_a) and integrated absorption intensities in 3600 cm.$^{-1}$ region (A) for various phenols* ($X{\cdot}C_6H_4{\cdot}OH$).

Group X	H	*p*-OMe	*p*-Cl	*m*-Cl	*m*-NO_2	*p*-NO_2
K_s (32·5°)	3·2	3·2	5·0	5·8	8·6	10·3
$10^{10}K_a$ (25°)	1·12	0·62	4·19	9·48	45·1	725
10^7A	5·8	5·6	6·6	6·7	8·7	8·5

explained by the increasing tendency of a phenol to associate with iodide ions in the way postulated above as its acid strength increases. 2,4,6-Tribromophenol is an apparent exception. The acid dissociation constant of this phenol is not available, but it is probably not less than 10^{-7} (for 2,4,6-trichlorophenol [6] pK_a at 25° = 6·46). However, comparison

FIG. 3. *Plots of* $(k_0 - k_2)/[ROH]$ *against* k_2 *for various phenols from data given in Table* 4.



(A) *Methanol*; (B) *phenol*; (C) m-*chlorophenol*; (D) m-*nitrophenol*; (E) p-*methoxyphenol*; (F) p-*chlorophenol*; (G) p-*nitrophenol*; (H) 2,4,6-*tribromophenol*.

of the appropriate plots in Fig. 3 shows that, despite its probable marked strength as an acid, 2,4,6-tribromophenol is only about as effective as methanol in retarding the iodine exchange. The relative ineffectiveness may arise from the presence of its large *ortho*-substituents, which prevent the close approach of an iodide ion and the hydrogen atom of the hydroxyl group.

More suitable than acid dissociation constants, for comparison with the association constants obtained from our kinetic experiments, would be the integrated intensities (A) of the infrared absorption band associated with the stretching vibration of the O–H bond,[7,8] because these depend only on the structure of the undissociated phenol molecules concerned. Relevant values for the integrated intensities of the absorption in the 3600 cm.$^{-1}$ region obtained by Stone and Thompson [7] are given in Table 5. Fig. 4, in which these values have been plotted against log K_s, shows an approximately linear relation and it may well be, therefore, that the formation of the ionic species (I, HOR)$^-$ involves a small change in O–H bond length, which is an important factor in determining the stability of such species.

Direct spectroscopic evidence for the existence of an interaction between anions and hydroxylic molecules has been obtained by Lund,[9] who found that solutions of hydroxylic compounds containing a small amount of tetrabutylammonium bromide possess an

[6] Tiessens, *Rec. Trav. chim.*, 1931, **50**, 112.
[7] Stone and Thompson, *Spectrochim. Acta*, 1957, **10**, 17.
[8] Brown, *Chem. Rev.*, 1958, **58**, 581; Flett, *Spectrochim. Acta*, 1957, **10**, 21.
[9] Lund, *Acta Chem. Scand.*, 1958, **12**, 298.

absorption band in the 3 μ region, the frequency of which is lower, and the integrated intensity larger, than those of the absorption band attributed to the free stretching vibration of the O–H bond. Several authors have pointed out, however, that the frequency of the absorption band corresponding to O–H stretching is generally lower and its integrated intensity higher, when the hydroxyl group forms part of some hydrogen-bonded system.[8,10] Hydrogen bonding between anion and hydroxyl group has, therefore, been invoked by Lund to account for his spectroscopic observations, and this would also explain why the shift in frequency of absorption produced by the addition of bromide ions increases with increasing acid strength of the hydroxylic compound. The apparent

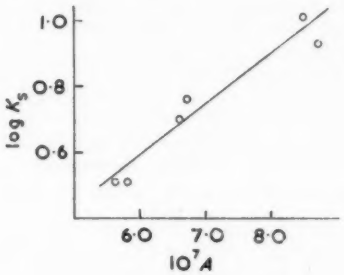


FIG. 4. *Plot of* $\log_{10} K_s$ *against integrated absorption intensity* (*A*) *for various phenols.*

integrated intensity of the absorption band attributed to the hydrogen-bonded anion complex also increases with increasing acid strength, except in the case of phenols with *ortho*-substituents. These behave anomalously in this respect, presumably for the same reason that 2,4,6-tribromophenol is relatively ineffective in retarding the iodine exchange reaction.

EXPERIMENTAL

Reagent-grade methyl cyanide was stored over anhydrous potassium carbonate for several days. It was then fractionated through a column packed with metal gauze rings, the fraction of b. p. 81·5—81·7° being retained for use. It was finally distilled under reduced pressure over phosphoric oxide to remove the last traces of water, and then refractionated.

After a preliminary treatment with anhydrous potassium carbonate, commercial methanol was distilled, then dried by Lund and Bjerrum's method [11] and fractionated. The fraction retained had b. p. 64·4—64·6°. The final water content of both purified solvents was about 0·02% by weight (Karl Fischer).

Radioactive iodine-131 was obtained as a solution of carrier-free sodium iodide in water. This was evaporated to dryness and then extracted with the appropriate dry solvent. n-Butyl iodide was purified as described in Part II.[1]

Phenols, except *m*-chlorophenol, were crystallised from light petroleum and then dried *in vacuo* over phosphoric oxide at room temperature. *m*-Chlorophenol could not be obtained as a solid product from solution. It was, therefore, purified by distillation under reduced pressure. M. p.s of purified phenols were within 1° of published values.

Kinetic procedure was that previously described.[1] Within a given experiment mean deviation of individual rate constants from the mean value of the rate constant was about 5%. Mean values of rate constants obtained from independent experiments did not usually differ by more than 10%.

We thank the Chemical Society for a grant to purchase the radioactive isotope, the University of Southampton for a research scholarship (to J. A. S.), and Dr. B. A. W. Simmonds for measurements of dielectric constant.

THE UNIVERSITY, SOUTHAMPTON. [*Received, June 8th*, 1960.]

[10] Barrow, *J. Phys. Chem.*, 1955, **59**, 1129.
[11] Lund and Bjerrum, *Ber.*, 1931, **64**, 210.

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43. *Internuclear Cyclisation. Part XVI.* Abnormal Reactions of Diazonium Salts from N-Alkyl-2-amino-2′- and -4′-methoxybenzanilides. A New Dienone–Phenol Rearrangement.*

By D. H. Hey, J. A. Leonard, T. M. Moynehan, and C. W. Rees.

Thermal decomposition of an aqueous solution of the diazonium sulphate from 2-amino-*N*-ethyl-4′-methoxybenzanilide (I) did not give the normal product of ring-closure, 10-ethyl-3-methoxyphenanthridone, but the spirodienone (III). This results from attack at the nuclear carbon atom *para* to the methoxyl group which also carries the *N*-ethyl group, and loss of the methyl from the methoxyl group. A similar reaction occurred with the corresponding *N*-methyl compound and with the 2′-methoxy-isomer of (I). The dienone (III), though remarkably stable to acid, underwent the dienone–phenol rearrangement to give 10-ethyl-3-hydroxyphenanthridone (IV), and was reduced to the dienol (VII). This dienol was rearranged by acid to 10-ethylphenanthridone (VI) and by alkali to *N*-ethyl-4′-hydroxybiphenyl 2-carboxyamide (VIII). Independent syntheses of these products of rearrangement are described and reaction mechanisms proposed.

In the extension of the Pschorr phenanthrene synthesis for the preparation of phenanthridones anomalous reactions have already been reported in the attempted preparation of 1-substituted 10-methylphenanthridones [1] and in the preparation of 10-phenylphenanthridones.[2] A further anomalous reaction has now been investigated which occurs in the attempted preparation of 1- and 3-methoxy-10-alkylphenanthridones.

It has already been reported [3] that 3-substituted 10-methylphenanthridones can be prepared in the normal manner from 4′-substituted 2-amino-*N*-methylbenzanilides *o*-NH_2·C_6H_4·CO·NMe·C_6H_4R-*p* where R is Me, Br, Cl, or NO_2. When the reaction was applied to 2-amino-4′-methoxy-*N*-methylbenzanilide a product was obtained which consistently gave an analytical result agreeing with a molecular formula with one carbon atom and two hydrogen atoms less than are required by the expected 3-methoxy-10-methylphenanthridone. After completion of these experiments it was reported by Govindachari and Arumugam [4] that 2-amino-*N*-ethyl-4′-methoxybenzanilide could be converted into 3-methoxy-10-ethylphenanthridone, although in a later communication [5] these authors, on the basis of the ultraviolet spectrum, stated that the product of this reaction could not be a derivative of phenanthridone. No alternative structure was put forward. In an attempt to explain these reactions further work has now been carried out on reactions with 2-amino-*N*-ethyl-2′-methoxybenzanilide, 2-amino-*N*-ethyl-4′-methoxybenzanilide (I), and 2-amino-4′-methoxy-*N*-methylbenzanilide.

The amines, 2-amino-*N*-ethyl-2′- and -4′-methoxybenzanilide, prepared as described by Govindachari and Arumugam,[4] were diazotised and decomposed thermally in aqueous acid. Purification of the products by chromatography yielded, together with the corresponding phenols, a single pure compound in each case, with melting points in agreement with those reported [4] but with differences in the ultraviolet absorption spectra.

Since the product, m. p. 137—138°, from 2-amino-*N*-ethyl-4′-methoxybenzanilide (I), was available in larger quantity further investigation centred upon this compound. The infrared spectrum showed peaks at 1668 and 1692 cm.$^{-1}$, which indicated the possible presence of a carbonyl group in addition to the expected amide-carbonyl function. This was confirmed by the formation of a dinitrophenylhydrazone and an oxime. Elementary

* Part XV, *J.*, 1959, 4110.

[1] Hey and Turpin, *J.*, 1954, 2471.
[2] Hey and Moynehan, *J.*, 1959, 1563.
[3] Heacock and Hey, *J.*, 1952, 4059; 1953, 3.
[4] Govindachari and Arumugam, *J. Sci. Ind. Res. India*, 1954, **13**, 694.
[5] Govindachari and Arumugam, *J. Sci. Ind. Res. India*, 1955, **14**, 250.

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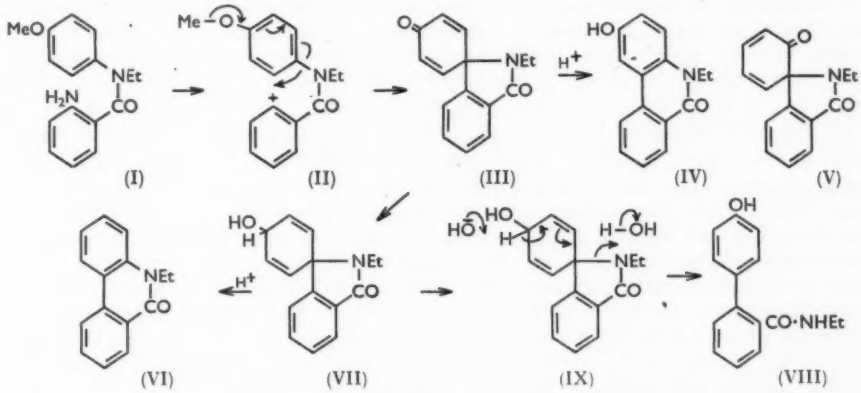
analysis and molecular-weight determination on the compound and its derivatives were consistent with a molecular formula $C_{15}H_{13}O_2N$, indicating the loss of a carbon atom from the original amine. That the *N*-ethyl group was not involved in this abnormal reaction was shown by the entirely analogous behaviour of the corresponding *N*-methyl compound. 4′-Methoxy-2-nitrobenzanilide was prepared from *o*-nitrobenzoyl chloride and *p*-anisidine and methylated with dimethyl sulphate, and the product was reduced catalytically to 2-amino-4′-methoxy-*N*-methylbenzanilide (I; Me instead of Et). Thermal decomposition of an aqueous solution of the corresponding diazonium sulphate gave a product, m. p. 217—218°, which exhibited very similar ultraviolet and infrared absorption to the *N*-ethyl compound, m. p. 137—138°, and similarly formed a 2,4-dinitrophenylhydrazone and had a molecular formula, $C_{14}H_{11}O_2N$, corresponding to the loss of one carbon atom. The strong absorption band at 1668 cm.$^{-1}$ due to the carbonyl group in these two products is in very close agreement with that attributed to the cross-conjugated carbonyl group of the cyclohexadienone system in, for example, steroidal dienones (1666—1663 cm.$^{-1}$),[6] geodin (1665 cm.$^{-1}$) and erdin (1667 cm.$^{-1}$),[7] and picrolichenic acid and its derivatives (1670—1665 cm.$^{-1}$).[8] Further, the ketone, on quantitative hydrogenation in ethanol over Adams catalyst, reacted with 1·95 mol. of hydrogen to yield a saturated ketone, m. p. 150°, with the carbonyl absorption shifted to 1717 cm.$^{-1}$ (saturated six-membered cyclic ketone). On the basis of these observations and the results, described below, of reactions carried out on these compounds, it is proposed that the product from (I) is 2-ethylisoindoline-1-spiro-1′-cyclohexadiene-3,4′-dione (III), and that from the isomeric *o*-methoxy-compound has the corresponding *o*-quinonoid structure (V). The latter product showed a broad maximum in the ultraviolet spectrum at 335 mμ (log ε 3·8) and a peak in the infrared spectrum at 1678 cm.$^{-1}$ characteristic of linearly conjugated cyclohexadienones.[6,8] The dienone (III) would result from electrophilic attack by the carbonium ion, formed from the diazonium ion by loss of nitrogen, at the carbon atom *para* to the methoxyl group, as shown in (II), the methyl group being lost, presumably as methanol. The alternative free-radical mechanism is perhaps less likely under the present conditions of thermal decomposition in aqueous acid; decomposition of the diazonium borofluoride by copper powder in acetone, conditions known to favour a radical mechanism, yields different products which will be described later.



Treatment of the dienone (III) with aqueous alkali yielded highly coloured decomposition products. Attempted reduction of it by the Wolff–Kishner method caused a breakdown of the molecule and the only product isolated was biphenyl-2-carboxylic acid. This

[6] Jones, Humphries, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 958.
[7] Barton and Scott, *J.*, 1958, 1767.
[8] Wachtmeister, *Acta Chem. Scand.*, 1958, **12**, 147.

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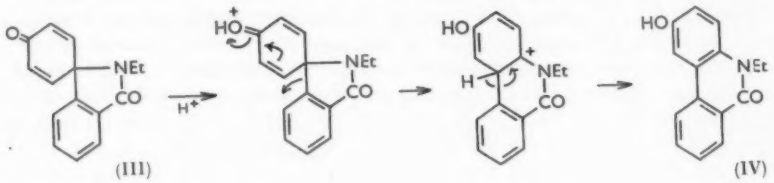
observation provided the first evidence of the existence of a bond between the two benzene rings. The dienone (III) was stable to prolonged boiling with concentrated hydrochloric acid, but 100% phosphoric acid at 170° isomerised it to a phenol, m. p. 260°, identified as 10-ethyl-3-hydroxyphenanthridone (IV), an independent synthesis of which is described below. Thus the spiran (III) has undergone the dienone–phenol rearrangement as illustrated. This is thought to be the first example of the dienone–phenol rearrangement involving a nitrogen-heterocyclic ring. The striking stability of the dienone (III) to acid is noteworthy; the compound was also stable to acetic anhydride containing sulphuric acid at room temperature, the usual conditions for this rearrangement,[9] but it rearranged when heated in this medium at 107° for 2 hr., to give 3-acetoxy-10-ethylphenanthridone. Reduction of the dienone (III) with sodium borohydride in methanol gave the alcohol (VII), m. p. 170—178°, which may be a mixture of stereoisomers. When heated with hydrochloric acid this alcohol underwent the dienol–benzene rearrangement,[10] analogous to the dienone–phenol rearrangement of (III), to give 10-ethylphenanthridone (VI). The



(III) (IV)

alcohol (VII) was isomerised by sodium hydroxide to a phenol, m. p. 184—185°, which yielded a diacetyl derivative. This product has been identified as *N*-ethyl-4′-hydroxybiphenyl-2-carboxyamide (IX) by mixed-melting-point determinations and infrared comparison with the independently synthesised product and its diacetyl derivative. Thus the rearrangement shown in (VIII) has occurred. 4′-Hydroxybiphenyl-2-carboxylic acid was prepared by heating fluorene-2-sulphonic acid with potassium hydroxide in diphenyl ether in a modification of Huntress and Seikel's method[11] and converted into its ethylamide *via* the acid chloride.

3-Nitrophenanthridone[12] was methylated, to yield 10-methyl-3-nitrophenanthridone identical with an authentic specimen,[3] thus confirming the position of the nitro-group. Diethyl sulphate converted 3-nitrophenanthridone into 10-ethyl-3-nitrophenanthridone, m. p. 216°, and an isomer, m. p. 159·5—161°, whose melting point was unaltered on crystallisation from ethanol, benzene, or light petroleum. This product was shown not to be 10-ethyl-1-nitrophenanthridone which would have been formed from any 1-nitro-isomer in the starting material. The *O*-ethyl compound, 9-ethoxy-3-nitrophenanthridine was synthesised from the 9-chloro-compound and sodium ethoxide and found to have m. p. 180—180·5°. The unknown product, m. p. 159·5—161°, was then subjected to chromatography on alumina which separated it into two compounds identical with 9-ethoxy-3-nitrophenanthridine and 10-ethyl-3-nitrophenanthridone respectively. The formation of a relatively large amount (27%) of the *O*-alkyl derivative with diethyl sulphate in alkaline-aqueous acetone, conditions which normally lead almost exclusively to *N*-alkylation, must presumably be attributed to electron-withdrawal from the amide-nitrogen atom by the *p*-nitro-group. Assignment of the *O*-ethyl and *N*-ethyl structure severally to these isomers was confirmed by their ultraviolet and infrared spectra. 10-Ethyl-3-nitrophenanthridone was reduced catalytically to the amine which was diazotised in sulphuric acid and converted into 10-ethyl-3-hydroxyphenanthridone (IV).

[9] Woodward and Singh, *J. Amer. Chem. Soc.*, 1950, **72**, 494.
[10] Gentle, Moss, Hertzog, and Hershberg, *J. Amer. Chem. Soc.*, 1958, **80**, 3702.
[11] Huntress and Seikel, *J. Amer. Chem. Soc.*, 1939, **61**, 816.
[12] Caldwell and Walls, *J.*, 1952, 2163.

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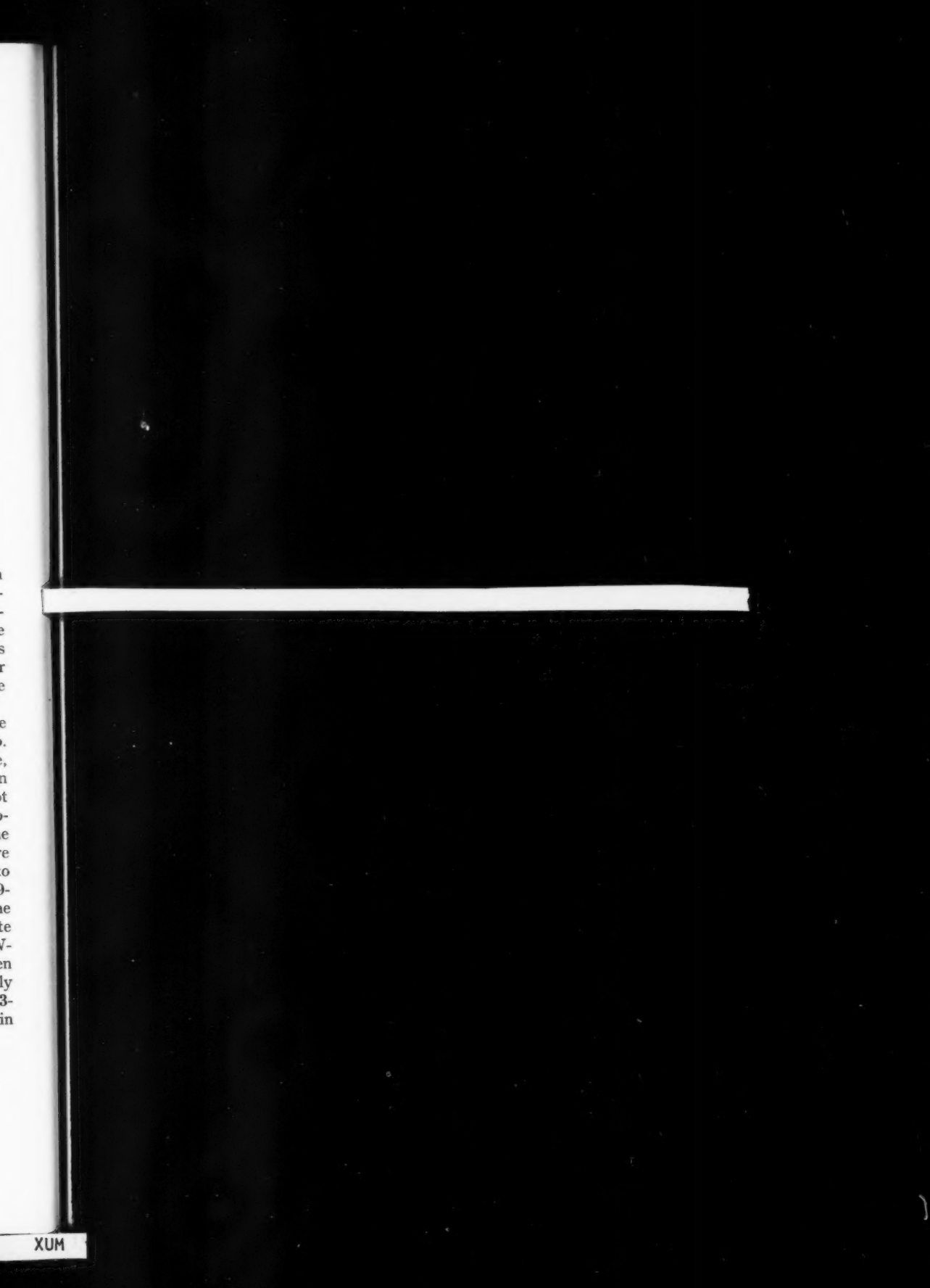

Vol. 1961, p. 234, lines 17 and 19. The roman figures IX and VIII should be interchanged.

Experimental

Ultraviolet spectra were determined for ethanol solutions, and infrared spectra for Nujol mulls.

2-Amino-*N*-ethyl-2′-methoxybenzanilide and 2-amino-*N*-ethyl-4′-methoxybenzanilide were prepared as described by Govindachari and Arumugam.[4] The former was obtained in plates, m. p. 99—101°, from aqueous methanol (Found: C, 71·2; H, 6·5. Calc. for $C_{16}H_{18}N_2O_2$: C, 71·1; H, 6·7%) and gave a benzoyl derivative, m. p. 133°; Govindachari and Arumugam [4] described this base as a viscous oil, which gave a benzoyl derivative, m. p. 133°. The second anilide was obtained in prisms, m. p. 101—102° (from ethanol) (Found: C, 71·2; H, 6·6%), from the corresponding 2-nitro-compound, which separated from ethanol in pale green needles, m. p. 74—75° (Found: C, 63·8; H, 5·3. Calc. for $C_{16}H_{16}N_2O_4$: C, 64·0; H, 5·3%). Govindachari and Arumugam [4] reported m. p. 102° for the base and m. p. 66° for the nitro-compound.

4′-Methoxy-2-nitrobenzanilide.—*o*-Nitrobenzoyl chloride (17 g.) in ether (50 ml.) was added dropwise to *p*-anisidine (10 g.) in a mixture of pyridine (15 ml.) and ether (50 ml.), and the mixture was boiled under reflux for 1 hr. The ether was removed and the residue poured into water. Crystallisation of the precipitated solid from ethanol gave *4′-methoxy-2-nitrobenzanilide* (18·5 g.) as yellow needles, m. p. 168—169° (Found: C, 61·9; H, 4·2. $C_{14}H_{12}N_2O_4$ requires C, 61·8; H, 4·4%).

2-Amino-4′-methoxy-N-methylbenzanilide.—4′-Methoxy-2-nitrobenzanilide (12 g.) in acetone (150 ml.) and 10% aqueous sodium hydroxide (150 ml.) was boiled under reflux and dimethyl sulphate (20 ml.) was added dropwise. The solution was boiled for 15 min. and then poured into water. The precipitate crystallised from ethanol, to give *4′-methoxy-N-methyl-2-nitrobenzanilide* (11·8 g.) as pale yellow needles, m. p. 144—146° (Found: C, 63·5; H, 5·0. $C_{15}H_{14}N_2O_4$ requires C, 62·9; H, 4·9%). A solution of this nitro-compound (4 g.) in benzene (100 ml.) with Raney nickel (4 g.) was hydrogenated at room temperature and pressure. Filtration, removal of the solvent, and recrystallisation of the residue from ethanol gave *2-amino-4′-methoxy-N-methylbenzanilide* (2·8 g.) in needles, m. p. 105—107° (Found: C, 70·0; H, 6·1. $C_{15}H_{16}N_2O_2$ requires C, 70·3; H, 6·2%).

Decomposition of the Diazonium Sulphate prepared from 2-Amino-N-ethyl-2′-methoxybenzanilide.—The amine (2·7 g.), suspended in 5% sulphuric acid (100 ml.), was diazotised at 0° with aqueous sodium nitrite (0·8 g. in 10 ml.). After being stirred at 0° for 1 hr. the mixture was gradually warmed to 70° and kept at that temperature for 1 hr. The mixture was then extracted with chloroform, and the extract was washed with aqueous sodium hydroxide and dried (Na_2SO_4). Removal of the solvent left a brown oil, which was dissolved in benzene–light petroleum and adsorbed on alumina (80 g.). Elution with benzene–light petroleum (800 ml.) gave gums (0·61 g.). Elution with benzene (1200 ml.) gave a brown solid gum (0·38 g.), which on crystallisation from light petroleum gave *2-ethylisoindoline-1-spiro-1′-cyclohexadiene-2′,3-dione* (V) (0·22 g.) in pale yellow needles, m. p. 117—118° (Found: C, 74·9; H, 5·1. $C_{15}H_{13}NO_2$ requires C, 75·3; H, 5·4%). Govindachari and Arumugam [4] obtained a compound, m. p. 117°, from a similar reaction. Further elution with benzene–ether, ether, and ethanol gave only tars (0·94 g.). The alkaline washings gave a yellow oil (0·17 g.).

Decomposition of the Diazonium Sulphate prepared from 2-Amino-N-ethyl-4′-methoxybenzanilide (I).—The amine (3 g.) was diazotised and decomposed as described for the previous experiment. The product in benzene was adsorbed on alumina (80 g.). Elution with benzene–light petroleum (1 : 1, 200 ml.; and 2 : 1, 500 ml.) gave gums (0·15 g.). Elution with benzene (1 l.) and benzene–ether (2 : 1; 300 ml.) gave a yellow solid, which crystallised from light petroleum, to give *2-ethylisoindoline-1-spiro-1′-cyclohexadiene-3,4′-dione* (III) (1·45 g.) in needles, m. p. 137—138° (Found: C, 75·4; H, 5·3; N, 5·8; O, 13·5%; *M*, 208. $C_{15}H_{13}NO_2$ requires C, 75·3; H, 5·4; N, 5·9; O, 13·4%; *M*, 239). Govindachari and Arumugam [4] obtained a compound, m. p. 138°, in smaller yield from a similar reaction. The *2,4-dinitrophenylhydrazone* separated from ethyl acetate in orange-red needles, m. p. 219—222° (Found: C, 59·8; H, 4·3%; *M*, 412. $C_{21}H_{17}N_5O_5$ requires C, 60·1; H, 4·1%; *M*, 419). The *oxime* separated from ethanol in prisms, m. p. 257° (decomp.) (Found: C, 70·0; H, 5·5. $C_{15}H_{14}N_2O_2$ requires C, 70·8; H, 5·5%). Elution with methanol gave a tar (0·08 g.). The alkaline washings, on acidification, gave *N-ethyl-2-hydroxy-4′-methoxybenzanilide* (0·5 g.), which separated from aqueous ethanol in needles, m. p. 133—134° (Found: C, 71·0; H, 6·5. $C_{16}H_{17}NO_3$ requires C, 70·8; H, 6·3%).

Decomposition of the Diazonium Sulphate prepared from 2-*Amino*-4′-*methoxy*-N-*methylbenzanilide*.—The amine (2 g.) was diazotised and decomposed, as described above for the *N*-ethyl compounds, and the product, in benzene, was adsorbed on alumina (80 g.). Elution with benzene (300 ml.) gave brown tars; more benzene (800 ml.) and benzene–ether (1 : 1; 600 ml.) gave a white solid which crystallised from ethanol to give 2-*methylisoindoline*-1-*spiro*-1′-*cyclohexadiene*-3,4′-*dione* (0·7 g.) in prisms, m. p. 217—218° (Found: C, 74·2; H, 4·9; N, 6·05. $C_{14}H_{11}NO_2$ requires C, 74·6; H, 4·9; N, 6·2%). The 2,4-*dinitrophenylhydrazone* crystallised from ethyl acetate in orange-red needles, m. p. 234—235° (Found: C, 58·7; H, 3·4; N, 17·3. $C_{20}H_{15}N_5O_5$ requires C, 59·2; H, 3·7; N, 17·3%). Elution with ether and methanol gave tars (0·13 g.). Acidification of the alkaline washings gave 2-*hydroxy*-4′-*methoxy*-N-*methylbenzanilide* (0·32 g.), which crystallised from aqueous ethanol in pale fawn plates, m. p. 152—153° (Found: C, 69·6; H, 5·8. $C_{15}H_{15}NO_3$ requires C, 70·0; H, 5·8%).

Reactions of 2-*Ethylisoindoline*-1-*spiro*-1′-*cyclohexadiene*-3,4′-*dione* (III).—(a) *Decomposition of the hydrazone*. The dienone (0·15 g.) was subjected to the Huang-Minlon modification of the Wolff–Kishner reduction.[13] The alkaline reaction mixture, on dilution with water and extraction with ether, gave only a yellow gum. The alkaline solution was acidified and extracted with ether. Concentration of the dried (Na_2SO_4) extract gave a solid, which crystallised from aqueous ethanol to give biphenyl-2-carboxylic acid (0·05 g.), m. p. and mixed m. p. 112—114°.

(b) *Reaction with phosphoric acid*. The dienone (0·2 g.), in 100% phosphoric acid (5 g.), was heated to 170° for 2 hr. The solid which was precipitated on addition of water crystallised from ethanol, to give 3-*hydroxy*-10-*ethylphenanthridone* (0·16 g.) in prisms, m. p. and mixed m. p. 260° (Found: C, 75·4; H, 5·5; N, 6·1. $C_{15}H_{13}NO_2$ requires C, 75·3; H, 5·4; N, 5·9%), $\lambda_{max.}$ 232, 239, 266, and 346 mμ (log ε 4·63, 4·61, 4·20, and 3·92). When this compound was left in acetic anhydride containing a few drops of concentrated sulphuric acid the *acetyl derivative* was obtained which crystallised from aqueous ethanol in needles, m. p. and mixed m. p. 150° (Found: C, 72·6; H, 5·3. $C_{17}H_{15}NO_3$ requires C, 72·6; H, 5·3%).

(c) *Reaction with acetic anhydride and sulphuric acid*. The dienone (0·052 g.) in acetic anhydride (3 ml.) was added to acetic anhydride (3 ml.) containing sulphuric acid (0·08 g.), and the mixture heated at 107° for 2 hr. and then poured into water (20 ml.). The 3-acetoxy-10-ethylphenanthridone (0·022 g.) which separated had m. p. and mixed m. p. 151°. More of this acetyl derivative (0·018 g.) was isolated from the aqueous solution, after neutralisation, by ether-extraction. When the dienone was treated similarly at 100° for 30 min., 23% was recovered, and after 22 hr. at room temperature 92% was recovered.

(d) *Action of sodium borohydride*. Sodium borohydride (0·1 g.) in methanol (15 ml.) was added dropwise to the dienone (0·2 g.) in methanol (20 ml.), and the mixture kept at room temperature for 2 hr. Water (25 ml.) was added and the solution saturated with potassium carbonate and extracted with ether. Evaporation of the dried (Na_2SO_4) extract and recrystallisation of the residue from aqueous ethanol and repeatedly from benzene gave 2-*ethyl*-4′-*hydroxyisoindoline*-1-*spiro*-1′-*cyclohexadien*-3-*one* (VII) (0·17 g.) in prisms, m. p. 170—178° (Found: C, 75·0; H, 6·2; N, 6·1. $C_{15}H_{15}NO_2$ requires C, 74·7; H, 6·2; N, 5·8%).

(e) *Hydrogenation*. The dienone (0·0955 g.) in ethanol (10 ml.), containing Adams catalyst (0·092 g.) and saturated with hydrogen, absorbed hydrogen (19·5 ml., 1·95 mol.) in 6 hr. The solution was filtered and evaporated and the residue crystallised from benzene–light petroleum, to give 2-*ethylisoindoline*-1-*spiro*-1′-*cyclohexane*-3,4′-*dione* (0·074 g.) in prisms, m. p. 149—150° (Found: C, 74·6; H, 7·5. $C_{15}H_{17}NO_2$ requires C, 74·1; H, 7·0%). This reduction product gave a positive test with the 2,4-dinitrophenylhydrazine reagent.

Reactions of 2-*Ethyl*-4′-*hydroxyisoindoline*-1-*spiro*-1′-*cyclohexadien*-3-*one* (VII).—(a) *Action of hydrochloric acid*. The dienol (0·2 g.) in concentrated hydrochloric acid (20 ml.) and ethanol (5 ml.) was boiled under reflux for 6 hr., poured into water, and extracted with chloroform. The extract was dried (Na_2SO_4) and the solvent removed. Crystallisation of the residue from light petroleum gave 10-ethylphenanthridone (0·16 g.), m. p. and mixed m. p. with an authentic specimen prepared by the method of Graebe and Wander,[14] 99—100° (lit.,[4,14] m. p. 89°).

(b) *Action of sodium hydroxide*. The dienol (0·2 g.) in a mixture of 10% aqueous sodium hydroxide (20 ml.) and ethanol (3 ml.) was boiled under reflux for 2 hr. The solution was acidified with hydrochloric acid and extracted with chloroform. The dried (Na_2SO_4) extract

[13] Huang-Minlon, *J. Amer. Chem. Soc.*, 1948, **70**, 2802.
[14] Graebe and Wander, *Annalen*, 1893, **276**, 245.

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was evaporated and crystallisation of the residue from aqueous ethanol gave N-*ethyl*-4′-*hydroxybiphenyl*-2-*carboxyamide* (0·16 g.) in plates, m. p. and mixed m. p. 184—185° (Found: C, 74·5; H, 6·4; N, 5·6. $C_{15}H_{15}NO_2$ requires C, 74·7; H, 6·2; N, 5·8%), $\lambda_{max.}$ 209 and 262 mμ (log ε 4·25 and 3·93). When this amide was heated in acetic anhydride containing a few drops of sulphuric acid on a water-bath for 30 min. a *diacetyl derivative* was formed, which crystallised from aqueous ethanol in plates, m. p. and mixed m. p. 103—104° (Found: C, 69·6; H, 5·8; N, 4·5. $C_{19}H_{19}NO_4$ requires C, 70·1; H, 5·8; N, 4·3%).

3-Nitrophenanthridone [12] was methylated with dimethyl sulphate in alkaline aqueous acetone to give 10-methyl-3-nitrophenanthridone, m. p. and mixed m. p. with an authentic specimen,[3] 253°.

Reaction of 3-*Nitrophenanthridone with Diethyl Sulphate.*—3-Nitrophenanthridone [12] (4 g.) in acetone (100 ml.) and 10% aqueous sodium hydroxide (50 ml.) was boiled under reflux and diethyl sulphate (6·7 ml.) was added dropwise. The solution was boiled for 25 min., cooled, and poured into water. The yellow precipitate was recrystallised successively from benzene, ethanol, and light petroleum (b. p. 100—120°), to give 10-*ethyl*-3-*nitrophenanthridone* (2·13 g.) as a pale yellow powder, m. p. 216° (Found: C, 66·8; H, 4·4; N, 10·4. $C_{15}H_{12}N_2O_3$ requires C, 67·2; H, 4·5; N, 10·4%), $\lambda_{max.}$ 226, 252, 263, and 341 mμ (log ε 4·41, 4·22, 4·21, and 3·96 respectively). The benzene mother-liquor, on concentration, gave a yellow powder (1·72 g.), m. p. 159·5—161° (Found: C, 67·0; H, 4·5; N, 10·5. Calc. for $C_{15}H_{12}N_2O_3$: C, 67·2; H, 4·5; N, 10·4%), $\lambda_{max.}$ 226, 232, 246, and 324 mμ (log ε 4·34, 4·35, 4·35, and 4·04 mμ respectively), whose m. p. was unaltered on crystallisation from ethanol or benzene and undepressed when mixed with 10-ethyl-3-nitrophenanthridone. This product (0·64 g.) in benzene was adsorbed on alumina and eluted with benzene (200 ml.) which gave a yellow solid (0·38 g.), m. p. and mixed m. p. with 9-ethoxy-3-nitrophenanthridine, 181°. Elution with benzene–ethanol (4 : 1; 300 ml.) gave a yellow solid (0·25 g.), m. p. and mixed m. p. with 10-ethyl-3-nitrophenanthridone, 216°.

9-*Ethoxy*-3-*nitrophenanthridine.*—3-Nitrophenanthridone (0·58 g.), phosphorus pentachloride (0·54 g.), and phosphoryl chloride (6 ml.) were heated at 130° for 5 hr. The mixture was poured on ice, and the solid which separated crystallised from benzene in needles of 9-*chloro*-3-*nitrophenanthridine* (0·49 g.), m. p. 251° (Found: C, 60·4; H, 2·8. $C_{13}H_7ClN_2O_2$ requires C, 60·1; H, 2·7%). A suspension of this chloro-compound (0·2 g.) in ethanol (40 ml.) was added to sodium ethoxide (from sodium, 0·24 g.) in ethanol (10 ml.), and the mixture boiled under reflux for 4 hr. The solution was concentrated, water was added, the mixture was extracted with ether, and the extracts were dried ($MgSO_4$). Removal of the ether gave 9-*ethoxy*-3-*nitrophenanthridine* (0·17 g.) which crystallised from ethanol (charcoal) in pale yellow needles, m. p. 180—180·5° (Found: C, 66·9; H, 4·7; N, 10·2. $C_{15}H_{12}N_2O_3$ requires C, 67·2; H, 4·5; N, 10·4%).

3-*Amino*-10-*ethylphenanthridone.*—10-Ethyl-3-nitrophenanthridone (0·83 g.) in ethanol (350 ml.) containing 10% palladised charcoal (0·1 g.) was shaken with hydrogen, uptake of which was complete in 2 hr. The *amine*, obtained in quantitative yield, crystallised from benzene–light petroleum (b. p. 60—80°) and then had m. p. 165·5° (Found: C, 74·9; H, 5·9; N, 11·9. $C_{15}H_{14}N_2O$ requires C, 75·6; H, 5·9; N, 11·8%).

10-*Ethyl*-3-*hydroxyphenanthridone.*—3-Amino-10-ethylphenanthridone (0·5 g.) in water (40 ml.) containing sulphuric acid (5 ml.) was diazotised at 0° with aqueous sodium nitrite (0·5 g. in 10 ml.) and stirred at 0° for 30 min. Water (25 ml.) was added, and the solution was gradually heated to 100°, kept at that temperature for 2 hr., made alkaline, filtered, and acidified. The orange precipitate crystallised from aqueous ethanol (charcoal) in pale orange prisms, m. p. and mixed m. p. 260° with the dienone–phenol rearrangement product described above. The infrared spectra of these two samples were identical. The acetyl derivative had m. p. and mixed m. p. 150°.

N-*Ethyl*-4′-*hydroxybiphenyl*-2-*carboxyamide.*—A suspension of sodium fluorene-2-sulphonate [15] (5 g.) in diphenyl ether (60 ml.) was added to a vigorously stirred emulsion of potassium hydroxide (12 g.) in hot diphenyl ether (70 ml.). After 4 hours' heating at 180° with stirring, the mixture was cooled and extracted with water (100 ml.), and the aqueous solution was acidified. The dark brown precipitate crystallised from water (charcoal) in pale yellow needles of 4′-hydroxybiphenyl-2-carboxylic acid (13%), m. p. 205·5°. The infrared absorption bands

[15] Wedekind and Stüsser, *Ber.*, 1923, **56**, 1561.

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at 759 (1,2-disubstituted benzene) and 830 cm.$^{-1}$ (1,4-disubstituted benzene) confirm the structure of this acid.

This acid (0·4 g.) was boiled under reflux with thionyl chloride (1 ml.) for 40 min. and excess of thionyl chloride was then removed by distillation with benzene. 33% Aqueous ethylamine (4 ml.) at 0° was added to the residue dissolved in acetone (2 ml.) at 0°, and the mixture was stirred for 30 min. The brown oil which separated crystallised from aqueous ethanol and then from ethanol–benzene in large prisms of the amide, m. p. and mixed m. p. 185° with the product of alkaline hydrolysis of the dienol (VII). These two specimens had identical infrared spectra. The diacetyl derivatives had m. p. and mixed m. p. 102—103°.

10-*Ethyl*-1-*nitrophenanthridone*.—1-Nitrophenanthridone [12] was ethylated with diethyl sulphate in the usual way, to give 10-*ethyl*-1-*nitrophenanthridone* which, crystallised from ethanol, had m. p. 127° (Found: C, 67·9; H, 4·6; N, 10·3. $C_{15}H_{12}N_2O_3$ requires C, 67·2; H, 4·5; N, 10·4%).

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44. *Organic Phosphorus Compounds. Part I. The Reaction of Dialkyl Methylphosphonates and Methylphosphonothionates with Inorganic Acid Chlorides.*

By ZVI PELCHOWICZ.

Dialkyl methylphosphonates are converted by thionyl chloride or, better, oxalyl chloride into alkyl methylphosphonochloridates. These ester chlorides are formed, under the same conditions, from the dialkyl methylphosphonothionates, sulphur being formed as by-product. The mechanism of the latter reaction is discussed.

IT has been observed [1] that reaction of phosphorus pentachloride with dialkyl methylphosphonates (I) gives methylphosphonyl dichloride in two steps, the time required for complete reaction increasing with increasing molecular weight of the alkyl group:

$$Me{\cdot}PO(OR)_2\ (I) + PCl_5 \longrightarrow Me{\cdot}POCl{\cdot}OR\ (II) + POCl_3 + RCl$$

$$Me{\cdot}POCl{\cdot}OR + PCl_5 \longrightarrow Me{\cdot}POCl_2 + POCl_3 + RCl$$

We have tried to use the differential reactivity of the two alkoxy-groups for the preparation of the synthetically valuable chlorides [2] (II). Hydrolysis with concentrated hydrochloric acid smoothly gave viscous products which were converted by thionyl chloride into the chlorides (II) in ~50% yield. From the infrared spectrum, it was concluded that the acidic viscous products are alkyl hydrogen methylphosphonates.[1a]

When the esters (I) were treated with boiling thionyl chloride, 80% yields of the chlorides (II) were obtained. The methyl and the isopropyl compound gave only polymers under these conditions, but use of oxalyl chloride gave good yields in all cases (Table 1). The analogous reaction with carbonyl chloride has been described.[3]

The parallel reaction of thionyl chloride with dialkyl methylphosphonothionates

[1] Pelchowicz, unpublished work.
[1a] Cf. Rabinowitz, *J. Amer. Chem. Soc.*, 1960, **82**, 4564.
[2] Cf. Hudson and Kealy, *J.*, 1956, 2463; Coe, Perry, and Brown, *J.*, 1957, 3604; Razumov, Mukhacheva, and Markovich, *Zhur. obshchei Khim.*, 1957, **27**, 2389; Hoffmann, Simmons, and Glunz, *J. Amer. Chem. Soc.*, 1957, **79**, 3570; de Roos, *Rec. Trav. chim.*, 1959, **78**, 145.
[3] Coe, Perry, and Brown, see ref. 2; Coe, Perry, and Sherlock, *J. Org. Chem.*, 1959, **24**, 1018.

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$Me{\cdot}PS(OR)_2$, best prepared [4] by the interaction of methylphosphonothionyl dichloride $Me{\cdot}PSCl_2$ with the sodium alkoxide in an excess of the alcohol, gave, not the expected ester chlorides of the thio-acid, but free sulphur and the ester chlorides (II). Analogous results were obtained with oxalyl chloride (Table 1); they may be explained by assuming that the starting compounds (III) are in equilibrium with the phosphonothiolates that are attacked as follows:

$$\underset{\text{(III)}}{Me{\cdot}PS(OR)_2} \rightleftharpoons Me{\cdot}PO(OR){\cdot}SR \xrightarrow{SOCl_2} Me{\cdot}POCl{\cdot}OR + [RS_2O{\cdot}Cl \longrightarrow] RCl + S + SO$$

$$\downarrow (COCl)_2$$

$$Me{\cdot}POCl{\cdot}OR + [RS{\cdot}CO{\cdot}COCl \longrightarrow] RCl + CO + COS$$

(Sulphur monoxide, SO, has been observed as an unstable intermediate in many reactions.[5]) It is reasonable that the more basic sulphur atom is attacked more quickly than oxygen. It may be pointed out that the infrared spectrum of dimethyl methylphosphonothionate does not show the frequency typical for the P=O bond (1270 cm.$^{-1}$),[6] but has a strong band in the 750 cm.$^{-1}$ region, in which the P=S frequency is known to lie.[7]

The above hypothesis is supported by the behaviour of dimethyl methylphosphonothionate towards phosphorus pentachloride. In this case, both the thiono- and the thioloform reacted, and the following reactions took place:

$$Me{\cdot}PO(OMe){\cdot}SMe + 2PCl_5 \longrightarrow Me{\cdot}POCl_2 + POCl_3 + 2MeCl + PCl_3 + S$$

$$Me{\cdot}PS(OMe)_2 + 2PCl_5 \longrightarrow Me{\cdot}PSCl_2 + 2POCl_3 + 2MeCl$$

It has been pointed out above that phosphorus pentachloride is capable of reacting with both ester groups of a phosphonate.

The toxicity (for rats) of some of the compounds (II) was determined. For the ethyl compound LD_{50} was 14 mg./kg., and for the isopropyl homologue 4·5 mg./kg. The higher toxicity of the secondary alkyl derivatives has been observed in similar cases.[8]

Experimental

Acid Hydrolysis of Diethyl Methylphosphonate.—This ester [9] (152 g., 1 mole) was mixed at room temperature with concentrated hydrochloric acid (300 ml.); a slightly exothermic reaction set in immediately; after refluxing for 1 hr., the excess of acid and water were removed *in vacuo*. The viscous residue was considered to be ethyl hydrogen methylphosphonate on the strength of its strongly acid reaction and the infrared bands (liquid film) at 3400, 3000 (Me), 1320 P–Me), 1230 (broad, P=O), 1030, 970, 900, 820, 780, and 720 cm.$^{-1}$.

For identification, it was treated in benzene (200 ml.) with thionyl chloride (113 g., 1 mole) in benzene (80 ml.) for 3 hr. The *ethyl methylphosphonochloridate* produced (yield, 62·5 g., 44%) distilled at 83—84°/23 mm. and had n_D^{25} 1·4320 (Found: Cl, 25·0. $C_3H_8ClO_2P$ requires Cl, 24·9%).

Reaction of Dialkyl Methylphosphonates with Thionyl Chloride.—A mixture of the dialkyl methylphosphonate (1 mole), in an equal volume of benzene, with thionyl chloride (2·5 moles) was refluxed for 3 hr., and then distilled *in vacuo*. The methyl and the isopropyl compound gave only polymers, but the following positive results were obtained: ethyl ester chloride, b. p. 83—84°/23 mm., n_D^{25} 1·4320 (yield, 80%); propyl ester chloride, b. p. 63°/4 mm., n_D^{19} 1·4378 (yield, 85%); n-butyl ester chloride, b. p. 70°/3 mm., n_D^{17} 1·4389 (yield, 87%).

Reaction of Dialkyl Methylphosphonates with Oxalyl Chloride.—To the dialkyl methylphosphonate (0·1 mole) in dry ether (150 ml.), oxalyl chloride (23·5 g., 0·115 mole), in ether (10 ml.),

[4] Kabachnik and Godovnikov, *Doklady, Akad. Nauk S.S.S.R.*, 1956, **110**, 217; Razumov, Mukhacheva, Zaikonnikova, Godovnikov, and Rizpolozhenzkii, *Khim. i Primenenie fosfororg, Soedin. Akad. Nauk S.S.S.R., Trudy 1-oi Conferents*, 1955, 205 (*Chem. Abs.*, 1958, **52**, 293); Hoffmann, Wadsworth, and Weiss, *J. Amer. Chem. Soc.*, 1958, **80**, 3945.

[5] See, *e.g.*, Schenk, *Z. anorg. Chem.*, 1933, **211**, 150; 1934, **220**, 268; 1936, **229**, 305; Woehler and Wegwitz, *ibid.*, 1933, **213**, 129.

[6] Corbridge, *J. Appl. Chem.*, 1956, **6**, 456.

[7] Pelchowicz, following paper; Hooge and Christen, *Rev. Trav. chim.*, 1958, **77**, 911; Gore, *Discuss. Faraday Soc.*, 1950, **9**, 138; Corbridge, ref. 6; Scott, Menefee, and Alford, *J. Org. Chem.*, 1957, **22**, 789, 792. Popov, Mastryukova, Rodionov, and Kabachnik, *Zhur. obshchei Khim.*, 1959, **29**, 1998.

[8] *E.g.*, Saunders and Stacey, *J.*, 1948, 695.

[9] *Org. Synth.*, 1951, **31**, 33.

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was added at 0° with stirring. The mixture was kept at room temperature for 24 hr., then evaporated to remove the solvent and the alkyl chloride formed, and distilled *in vacuo*. The results are summarized in Table 1.

TABLE 1. *Alkyl methylphosphonochloridates* (II).

R	B. p./ mm.	n_D	d_4	$[R_L]_D$ calc.	$[R_L]_D$ found	Cl (%) calc.	Cl (%) found	Yield (%) (I) + $(COCl)_2$	Yield (%) (III) + $SOCl_2$	Yield (%) (III) + $(COCl)_2$
Me	73°/22	1·4395 (18°)	1·3005 (16°)	25·52	26·00	27·7	27·6	85	50	85
Et	83°/21	1·4385 (18°)	1·2095 (16°)	30·14	30·97	24·9	24·8	88	72	87
Pr^n	94°/21	1·4378 (18°)	1·1602 (16°)	34·76	35·41	22·7	22·7	87	80	95
Pr^i	83°/22	1·4285 (23°)	1·1479 (21°)	34·76	35·50	22·7	22·8	61	62	75
Bu^n	105°/19; 70°/3	1·4388 (15°)	1·1225 (16°)	39·38	39·77	20·8	20·9	93	82	91

Methylphosphonothionyl dichloride was prepared as follows[3]: Methylphosphonyl dichloride[10] (133 g., 1 mole) was refluxed with phosphorus pentasulphide (36 g., 0·25 mole) for 3—4 hr., until a dark homogeneous mass was formed. The product was distilled *in vacuo*, and the distillate washed three times with water (200 ml.), dried (Na_2SO_4), and fractionated; the product (124 g., 83%) had b. p. 154°/760 mm., 44—45°/9 mm., m. p. −25·8°, n_D^{25} 1·5485, d_4^{25} 1·4178, $[R_L]_D$ 33·43.

The dialkyl methylphosphonothionates were prepared according to directions of Hoffmann;[4] it was advantageous to wash the esters with water before distillation. Their constants were practically identical with those recorded in the literature. The molecular refractivities are summarized in Table 2.

TABLE 2. *Molecular refractivity of* Me·PS(OR)$_2$.[11]

R	n_D	d_4^{25}	$[R_L]_D$ calc.	$[R_L]_D$ found	R	n_D	d_4^{25}	$[R_L]_D$ calc.	$[R_L]_D$ found
Me ...	1·4738 (25°)	1·1375	34·40	34·57	Pr^i ...	1·4570 (20°)	0·9889	52·88	53·83
Et ...	1·4630 (22°)	1·0510	43·64	43·94	Bu^n ...	1·4642 (17·5°)	0·9820	62·11	62·70
Pr^n ...	1·4640 (18°)	1·0097	52·88	53·46					

Reactions of Dialkyl Methylphosphonothionates.—(i) *With thionyl chloride.* To thionyl chloride (2·5 moles), the ester (1 mole) was added at room temperature. The spontaneous reaction, which was accompanied by precipitation of sulphur, was completed by refluxing the mixture for 2 hr. The sulphur was filtered off, and the alkyl methylphosphonochloridate fractionated (see Table 1).

(ii) *With oxalyl chloride.* To a solution of the ester (1 mole) in ether (200 ml.), oxalyl chloride (1·5 moles for the methyl ester, 1·75 moles for the ethyl and the isopropyl ester, 2 moles for the propyl and the butyl ester) in ether (200 ml.) was added at room temperature. After 24 hr. at room temperature, the ether and the excess of oxalyl chloride were distilled off, and the product was fractionated *in vacuo* (see Table 1).

Reaction of Dimethyl Methylphosphonothionate with Phosphorus Pentachloride.—In a 2-l. flask, chlorine was passed through a solution of phosphorus trichloride (275 g., 2 moles) in carbon tetrachloride (350 ml.). When all the trichloride had been converted into the pentachloride, the mixture was refluxed for 1 hr., and dimethyl methylphosphonothionate (142 g., 1 mole) added with cooling and stirring. A lively reaction took place, accompanied by dissolution of the phosphorus pentachloride and appearance of a yellow colour. The mixture was refluxed for 2 hr. and distilled quickly, in the later stages *in vacuo*. The residue consisted of sulphur, and also from the deep yellow distillate sulphur crystallised. Fractional distillation yielded: (1) carbon tetrachloride, containing 96·2 g. (0·7 mole) of phosphorus trichloride; (2) phosphorus oxychloride, 184 g. (1·2 moles); (3) b. p. 122—125°, 10 ml. (14·2 g.), a mixture of phosphorus oxychloride and $PSCl_3$; (4) b. p. 154° (13·3 g.), a mixture of $CH_3{\cdot}POCl_2$ and $CH_3{\cdot}PSCl_2$; by washing with cold water, the former was destroyed, whilst the latter (7·5 g.) remained unattacked (b. p. 154°, n_D^{25} 1·5485. Found: S, 21·50. Calc. for CH_3Cl_2PS: S, 21·47%), (5) b. p. 163—165° (86·5 g., 65%), methylphosphonyl dichloride.

ISRAEL INSTITUTE FOR BIOLOGICAL RESEARCH,
NESS-ZIONAH, ISRAEL.

[*Received, July 13th*, 1959.]

[10] Kinnear and Perren, *J.*, 1952, 3437.

[11] As atomic refractions for doubly bound sulphur and phosphorus, the values 9·70 and 4·27, respectively, were used.

45. *Studies on Organic Phosphorus Compounds. Part II.* Dialkyl Phosphorothioites and Their Reaction with Chloral.*

By Zvi Pelchowicz.

The reaction of dialkyl phosphorothioites with chloral is accompanied by rearrangement and dehydrohalogenation and yields *OO*-dialkyl *S*-(2,2-dichlorovinyl) phosphorothioates (IV). The structures of the starting materials and the products are discussed on the basis of their infrared spectra and molecular refraction. The effect of the compounds (IV) on mice and flies has been investigated.

Dialkyl phosphites react with chloral to give compounds (I), which are valuable insecticides.[1] It seemed of interest to study the corresponding reaction of dialkyl phosphorothioites (II), which can be prepared by reaction of dialkyl phosphorochloridites $(RO)_2PCl$ with hydrogen sulphide in the presence of a tertiary base [2] or by reaction of a suitable alcohol with phosphorus trisulphide (P_4S_6).[3] Reaction of the thioesters (II) with chloral did not give the expected compounds (III) but was accompanied by rearrangement and dehydrohalogenation, yielding *OO*-dialkyl *S*-(2,2-dichlorovinyl) phosphorothioates (IV).

The analogous reaction of compounds (I) takes place only when they are treated with an alkaline reagent. If the two rearrangements are analogous, the hydroxyl-oxygen atom of (I) will appear in the rearranged product in the P=O grouping. The structure of the compounds (II) and (IV) follows from the molecular refraction and the infrared spectrum.

$(RO)_2PO{\cdot}CH(OH){\cdot}CCl_3$ (I) $(RO)_2PHS$ (II) $(RO)_2PS{\cdot}CH(OH){\cdot}CCl_3$ (III)

(IV) $(RO_2)PO{\cdot}S{\cdot}CH{:}CCl_3$ $(RO)_2PS{\cdot}O{\cdot}CH{:}CCl_2$ (IVa)

The P=S double bond, which in $PSCl_3$ has been found to have a very broad band with its centre at 754 cm.$^{-1}$ and a frequency [5] between 535 and 745 cm.$^{-1}$, appears also in the infrared spectra of dimethyl, diethyl, and dipropyl phosphorothioite; these spectra do not contain the bands (2550—2600 cm.$^{-1}$) characteristic of the S–H stretching vibration,[6] but show the very distinct P–H bands [6] at 2400 cm.$^{-1}$ and the P–O–C vibration [7] around 1000 cm.$^{-1}$. The structure of the dialkyl phosphorothioites (II) is, therefore, analogous to that of the dialkyl phosphites.[8]

In the infrared spectrum of the condensation products (IV) the following bands have been observed: (IV; R = Me) 3550, 3100, 3000, 2900, 1560, 1450, *1270*, *1185*, *1025* (broad), *915*, *825*, *795*, *655* (italics denote strong bands); (IV; R = Et) *3000*, 1560, (1475), 1450, 1390, *1270*, 1160, *1000* (very broad), *915*, 810 (broad), 655; (IV; R = Pr^n) *3000*, 1525, 1470, 1390, *1270*, 1150, *1000* (broad), 915, 855, 815, 745, 655.

Whilst the P=S band is absent, all the spectra exhibit the characteristic vibration of the P=O bond (1270 cm.$^{-1}$). The bands in the 1400—1560 region are due to the C=C double bond, and the broad bands around 1000 cm.$^{-1}$ to the P–O–C vibration. The band

* Part I, preceding paper.

[1] Lorenz, Henglein, and Schrader, *J. Amer. Chem. Soc.*, 1955, **77**, 2554; Zbirovsky and Ettel, *Sbornik vysoke skoly chem.-technol v Prase*, 1957, 253 (*Chem. Abs.*, 1959, **53**, 6057).

[2] Sallman, U.S.P. 2,805,241 (*Chem. Abs.*, 1958, **52**, 2048).

[3] Kabachnik and Mastryukova, *Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk*, 1952, 727.

[4] Barthel, Alexander, Giang, and Hall, *J. Amer. Chem. Soc.*, 1955, **77**, 2424.

[5] Hooge and Christen, *Rec. Trav. chim.*, 1958, **77**, 911.

[6] Jones and Sandorfy, "Chemical Applications of Spectroscopy," in "Technique of Organic Chemistry," Interscience Publ. Inc., New York, 1956, Vol. VIII, p. 247.

[7] Bergmann, Littauer, and Pinchas, *J.*, 1952, 847.

[8] Daasch, *J. Amer. Chem. Soc.*, 1958, **80**, 5301; Kabachnik and Mastryukova, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1953, 163 (*Chem. Abs.*, 1954, **48**, 3243). This has recently been confirmed by measurements of the nuclear magnetic resonance (Yamasaki, *Sci. Reports Res. Inst. Tohôku Univ.*, Ser. A, 1959, **11**, 73).

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at 655 cm.$^{-1}$ may be assigned to the S–C stretching vibration.[9] The absence of the P=S frequency precludes formula (IVa) which would be as compatible as (IV) with the observed values for the molecular refraction (see Table 3).

Biological tests with the compounds of formula (IV) were carried out with male, white mice and with flies, both a susceptible and a D.D.T.-resistant strain of *Musca vicina* Macq. Quantities of the order of LD_{50} diluted with saline and injected into white mice produced after 7—10 min. the symptoms of cholinesterase poisoning (tremors, salivation, lachrymation, convulsions, and dyspnoea), followed by coma and death. Blood and brain of animals poisoned with 2 LD_{50} were tested for cholinesterase (ChE); the results are summarised in Table 1.[10] The method used in the fly tests has been described by Tahori.[11] Benzene solutions of the compounds were applied topically to groups of 25 houseflies, and

TABLE 1. *Toxicity of compounds* (IV).

		Mice			Flies, insecticidal activity (mg./fly)	
		Time of death	% of residual ChE			
R	LD_{50} (mg./kg.)	(min.)	blood	brain	Susceptible	Resistant
Me	83	10—40	45—74	60—100	0·08	0·12
Et	30·6	10—20	46—55	40—50	0·03	0·04
Pr^n	80	30—40	9—23	5—20	0·15	0·20
Ester (I) [12]	15					

mortality counts taken after 24 and 48 hr.; each compound was tested in at least four concentrations and in quintuplicate. The results are listed in Table 1.

It is noteworthy that the toxicity of the compounds does not parallel the molecular weight. Both for mice and flies, the ethyl is much more toxic than either the methyl or the propyl compound. The sulphur compounds (IV) are much less toxic than the oxygen esters (I). It is further noteworthy that the most toxic substance does not necessarily reduce the amount of cholinesterase in blood or brain in the most pronounced manner. This is a further indication that the toxicity of the compounds is not, or at least not wholly, based on their anticholinesterase activity.

EXPERIMENTAL

Preparation of Dialkyl Phosphorothioites (II).—*Method* 1. Diethyl phosphorochloridite (72 g.), pyridine (37 g.), and light petroleum (450 ml.) were introduced into a nitrogen-filled flask. Hydrogen sulphide was then passed through the stirred mixture so that the gas was absorbed completely. When the exothermic reaction subsided and the gas was no longer absorbed, the pyridinium chloride formed was filtered off, and the filtrate distilled; diethyl phosphorothioite had b. p. 86·9°/26 mm. (yield, 81%).

Method 2. Phosphorus trisulphide (1 mol.) was refluxed with the alcohol (10 mol.) for varying periods: *viz.*, methanol, 20; ethanol, 12—15; propanol, 10; butanol, 9 hr. The product was isolated by distillation, yields being about 20%.

TABLE 2. *Dialkyl phosphorothioites* (II).

					S (%)	
R	Method	B. p./mm.	Yield (%)	n_D	found	calc.
Me	2	69—70°/30	20	1·4748 (27·0°)	25·1	25·1
Et	1, 2	86·9°/26	81; 20	1·4631 (27·0°)	20·8	20·7
Pr^n	1, 2	112°/30	73; 20	1·4543 (30·5°)	17·0	17·4
Pr^i	1, 2	95°/26	34; 20	1·4492 (39·0°)	17·6	17·4
Bu^n	1, 2	148°/32	83; 20	1·4510 (30·5°)	15·2	15·1

The dialkyl phosphorothioites are colourless oils, which can be treated with water without causing dissolution or decomposition. In this way, dialkyl phosphites, which might contaminate the products, can be eliminated easily. These products are reported in Table 2.

[9] Sheppard, *Trans. Faraday Soc.*, 1950, **46**, 429.
[10] See Edery and Schatzberg-Porath, *Science*, 1958, **128**, 1137.
[11] Tahori, *J. Econ. Entomol.*, 1955, **48**, 638.
[12] van Asperen, *Ent. Expt. and Appl.*, 1958, **1**, 130.

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OO-*Dialkyl* S-(2,2-*Dichlorovinyl*) *Phosphorothioates* (IV).—Diethyl phosphorothioite (0·9 mole) was added to chloral (1 mole), at 60°. The exothermic reaction was accompanied by a transient violet-red colour; the temperature of the mixture was kept below 80°. The yellowish product

TABLE 3. OO-*Dialkyl* S-(2,2-*dichlorovinyl*) *phosphorothioates* (IV).

R	B. p./mm.	Yield (%)	*n*	*d*	MR, fd.	$[R_L]_D$ [13] calc. (IV)	calc. (IVa)	Cl (%) calc.	Cl (%) found	S (%) calc.	S (%) found
Me	113—115°/2	70	1·5235 (23·5°)	1·4442 (22·0°)	50·30	49·93	48·78	30·0	29·7	13·5	13·7
Et	130°/5	70	1·5020 (25·0°)	1·3119 (22·0°)	59·60	59·76	58·00	26·8	26·5	12·1	12·4
Pr^n	135°/2	30	1·4870 (25·0°)	1·2350 (23·0°)	68·35	68·40	67·24	24·2	24·1	10·9	11·1

was evacuated and distilled *in vacuo*, in the presence of a small quantity of quinol; the diethyl product had b. p. 130°/5 mm. (yield 70%). Other esters were obtained similarly and the properties are summarized in Table 3.

Thanks are tendered to Dr. Edery and Dr. Tahori, of this Institute, for biological evaluation of our compounds.

THE ISRAEL INSTITUTE FOR BIOLOGICAL RESEARCH,
NESS ZIONAH, ISRAEL. [*Received, July 13th*, 1959.]

[13] For doubly bound phosphorus and sulphur, the atomic refractions 9·70 and 4·27 were used; for doubly bound oxygen the value characteristic for carbonyl-oxygen (2·21).

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46. *Synthesis of Antiviral Agents. Part I. Heterocyclic Compounds Related to Isatin 3-Thiosemicarbazone.*

By P. W. SADLER.

Diphenyl derivatives of dihydrothio-1,2,4-triazine and 5-thio-2-triazoline have been synthesised and found to have no antiviral activity; indole-5-thioamide is also inactive. Some ring-substituted *N*-alkylisatin 3-thiosemicarbazones showed high activity.

1-ETHYLISATIN 3-THIOSEMICARBAZONE (I; R = Et), the most potent antiviral agent yet discovered, is under clinical trial.[1,2] As very few heterocyclic thiosemicarbazones possess detectable antiviral activity, the possibility arises that 1-alkylisatin 3-thiosemicarbazones owe their high activity to conversion *in vivo* into tricyclic dihydrothioindolotriazines (II). Both the α-carbonyl and the terminal amino-group (*i.e.*, the groups necessary for cyclization) are essential for the retention of antiviral activity.[1] Although the 2-carbonyl group is part of an amide grouping, there are cases in which both carbonyl groups of isatin take part in a reaction. Thus 1-methylisatin with two mols. phenylmagnesium bromide gives a mixture of indoxyl and oxindole derivatives;[3] 1-acetylisatin gives a dioxime[4] and bisphenylhydrazone;[5] isatin gives a dioxime,[6] dianilide,[7] and a quinoxaline derivative.[8]

Attempts to prepare a compound (II; R = Me) by heating 1-methylisatin 3-thiosemicarbazone above its melting point or by reaction with strong acids failed. Heating 1-ethylisatin 3-thiosemicarbazone under reflux in butanol for 14 days produced only 1-ethylisatin 3-4′-butylthiosemicarbazone. No antiviral activity was detected in any of

[1] Bauer and Sadler, *Brit. J. Pharmacol.*, 1960, **15**, 101
[2] Bauer and Sadler, *Lancet*, 1960, **1**, 1110.
[3] Witkop and Ek, *J. Amer. Chem. Soc.*, 1951, **73**, 5664.
[4] Schunk and Marchlewski, *Ber.*, 1895, **28**, 543.
[5] Panaotovik, *J. prakt. Chem.*, 1886, **33**, 58.
[6] Reissert and Hessert, *Ber.*, 1924, **57**, 964.
[7] Reissert and Hoppmann, *Ber.*, 1924, **57**, 972.
[8] Buraczewski and Marchlewski, *Ber.*, 1901, **34**, 4010; Korczynski and Marchlewski, *Ber.*, 1902, **35**, 4334.

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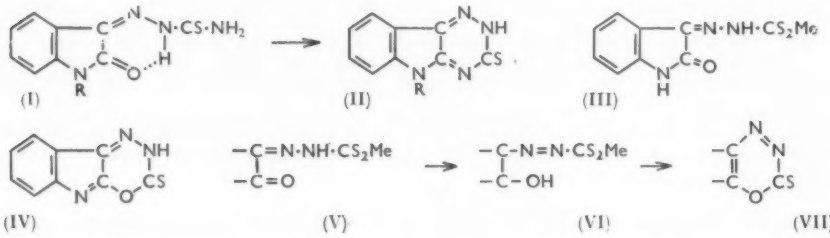
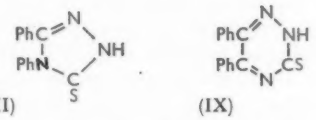
the decomposition products formed in these reactions. Cyclisation of isatin 3-*N'*-methylthiothiocarbonylhydrazone (III) to the oxadiazine (IV) has been reported by Guha and Guha.[9] The reaction is a general one; for example, phenanthraquinone and acenaphthaquinone form the thioesters (V), which, in the azo-form (VI) lose methanethiol, giving the 1,3,4-oxadiazines (VII). Repetition of the preparation of compound (IV) yielded a



compound of melting point similar to that reported,[9] but analysis indicated structure (III), which was confirmed when the infrared spectra disclosed the presence of two imino-groups and a carbonyl group. Similarly 1-methylisatin produced only a derivative (V), and none of the oxadiazine (VII). However, heating the hydrazone (III) in acetic anhydride yielded its acetyl derivative and this had a melting point similar to that reported for the acetyl derivative of the oxadiazine (IV);[9] the benzoyl derivative of compound (IV) was obtained in small yield from the hydrazone (III) by the Schotten–Baumann process. This is analogous to the action of excess of benzoyl chloride on 1-benzoyl-4-phenylthiosemicarbazide which cyclises with loss of water to form 3,4-diphenyl-5-thio-2-triazoline (VIII). The corresponding triazine (IX) is formed more readily, by heating an ethanolic solution of benzil monothiosemicarbazone under reflux. From this it follows that the 2-carbonyl group of isatin is not sufficiently reactive to permit cyclisation of its monothiosemicarbazone and methylthiothiocarbonylhydrazone under mild conditions, which is a characteristic of some other α-diketones. Further evidence against the postulated conversion of 1-alkylisatin 3-thiosemicarbazones *in vivo* into indolotriazines is that neither the thiotriazoline (VIII) nor the dihydrothiotriazine (IX) possesses antiviral activity. This, coupled with the lack of direct evidence for the formation of (II) from (I), render this mechanism unlikely.



As the formation of stable tricyclic compounds from isatin 3-thiosemicarbazones could not be demonstrated, a study was made of the configuration of their hydrogen-bonded forms. Infrared spectra indicate the presence of both inter- and intra-molecular bonding, the latter being more marked in the 1-alkyl derivatives (I). Similar resonance stabilising of six-membered hydrogen-bonded rings has been demonstrated for isatin 3-oximes.[10] A similar hydrogen-bonded structure is indicated for isatin 2-thiosemicarbazone, but as this has no antiviral activity, the possibility arises that the steric relation of the thioamide group to the ring-nitrogen atom is important. 5-Thiocarbamoylindole (X) has the thioamide group in the required position but has no antiviral activity. Adrenochrome monothiosemicarbazone (XI) is also inactive.

[9] Guha and Guha, *J. Indian Chem. Soc.*, 1927, **4**, 239.
[10] O'Sullivan and Sadler, *J. Org. Chem.*, 1957, **22**, 283.

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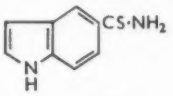
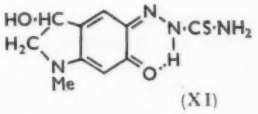
In view of the high antiviral activity of compounds (I), some derivatives having a substituent also in the benzene ring have been prepared. 3-Thiosemicarbazones of 5-fluoro-1-methyl- and 1-ethyl-5-fluoro-isatin retained the high activity, and the compound having



(X)



(XI)

a 1,7-trimethylene bridge had activity approximately the mean of the values for the 1- and the 7-ethyl compound.

Experimental

Spectra were determined by using a Perkin-Elmer 21 double-beam recording spectrometer with a rock-salt prism.

Test of Antiviral Activity.—The IHD strain of neurotropic vaccinia virus adapted to intracerebral passage in mice was used. The mean reciprocal survival time of mice infected intracerebrally with neurovaccinia virus has a linear regression upon the logarithm of the dilution of virus used for infection; an active compound causes a significant reduction of the mean reciprocal survival time over a wide range of virus doses.[11] Compounds which gave no significant reduction of the mean reciprocal survival time at a dose of 125 mg./kg. in mice infected intracerebrally with about 1000 LD 50 of neurovaccinia virus were considered to be inactive.

1-*Ethylisatin* 3-4′-*Butylthiosemicarbazone*.—1-Ethylisatin 3-thiosemicarbazone (2 g.) was refluxed in butanol (125 c.c.) for 14 days. When the solution was concentrated to 50 c.c. and chilled, 0·1 g. of unchanged thiosemicarbazone, m. p. 204°, was recovered. Further concentration produced crystals which on recrystallisation from ethanol afforded the red 4′-*butyl derivative*, m. p. 83° (Found: C, 59·3; H, 6·2; S, 10·2. $C_{15}H_{20}N_4OS$ requires C, 59·2; H, 6·6; S, 10·5%).

Isatin 3-N′-*Methylthiothiocarbonylhydrazone* (III).—Isatin (1·5 g.) and methylthiothiocarbonylhydrazine (1·3 g.) were heated in acetic acid under reflux; a deep yellow precipitate of the *hydrazone* was obtained which recrystallised from acetone as pale orange needles, m. p. 227° (Found: C, 47·9; H, 3·5; S, 25·5. $C_{10}H_9N_3OS_2$ requires C, 47·8; H, 3·6; S, 25·5%). When this was heated under reflux in acetic anhydride for 20 min., and the product was recrystallised from ethanol, the *acetyl derivative* formed white needles, m. p. 165° (Found: S, 22·2. $C_{12}H_{11}N_3O_2S_2$ requires S, 21·9%). The acetyl derivative of the oxatrazine (IV) (calc. for $C_{11}H_7N_3O_2S$: S, 13·1%) is reported to have m. p. 162°. Schotten–Baumann benzoylation of the hydrazone (III) gave the benzoyloxathiazine as white plates, m. p. 227° (lit., m. p. 228—229°).

1-*Methylisatin* 3-*methylthiothiocarbonyl hydrazone* was obtained similarly as orange needles, m. p. 171° (Found: C, 49·7; H, 4·0; S, 23·5. $C_{11}H_{11}N_3OS_2$ requires C, 49·8; H, 4·2; S, 24·1%).

Adrenochrome Monothiosemicarbazone (XI).—Adrenaline (5 g.) in chilled water (100 c.c.) containing 20N-formic acid (2 c.c.) was added with rapid stirring to silver oxide (20 g.) in chilled water (40 c.c.). The mixture was stirred vigorously for 2 min. Ice (50 g.) was added and the mixture filtered into a solution of thiosemicarbazide (3·7 g.) in the minimum quantity of warm water.[12] The flocculent red *thiosemicarbazone* was collected, washed with water, and recrystallised from ethanol (1 l.), giving red needles, m. p. 220° (Found: C, 47·5; H, 4·6. $C_{10}H_{12}N_4O_2S$ requires C, 47·6; H, 4·8%).

2,3-*Dihydro*-5,6-*diphenyl*-3-*thio*-1,2,4-*triazine* (IX).—Benzil (21·1 g.) and thiosemicarbazide (9·1 g.) were heated under reflux in ethanol (200 c.c.) for 24 hr. The orange precipitate was removed from the cooled mixture, suspended in water (200 c.c.) at 80° for 20 min., collected again, and washed with ether, leaving the *triazine derivative* (13·7 g.) as orange needles which, recrystallised from butanol, had m. p. 226° (Found: C, 67·8; H, 4·1; N, 16·2; S, 12·1.

[11] Bauer, *Brit. J. Exp. Path.*, 1958, **39**, 480.
[12] Fleischhaker and Barsel, U.S.P. 2,712,024/1955.

$C_{15}H_{11}N_3S$ requires C, 67·9; H, 4·2; N, 15·9; S, 12·1%). Chilling the ethanolic filtrate produced benzil monothiosemicarbazone as white needles (1·6 g.), m. p. 188° unchanged on crystallization from ethanol (Found: C, 63·8; H, 4·8. Calc. for $C_{15}H_{13}N_3OS$: C, 63·5; H, 4·6%). Concentration of the final mother-liquors produced a mixture (7·5 g.) of the two products from which the thiosemicarbazone was removed by continuous extraction with ether; neither fractional crystallisation from ethanol nor the action of sodium carbonate solution effected separation.[13] Heating the thiosemicarbazone at 110° at 0·05 mm. for 3 hr. converted it quantitatively into the triazine.

3,4-*Diphenyl*-5-*thio*-2-*triazoline* (VIII).—Benzhydrazide (4·5 g.) was added to phenyl isothiocyanate (4·5 g.) in ethanol (20 c.c.) and left overnight, giving 1-benzoyl-4-phenylthiosemicarbazide (5·3 g.) as needles, m. p. 164°, which was then heated with a large excess of benzoyl chloride for 3 min. on a boiling-water bath. Ether was added to the chilled mixture, and the precipitate collected and washed with ether. Crystallisation from ethanol gave needles of the triazoline, m. p. 284° (lit.,[14] m. p. 287°).

1,2,5,6-*Tetrahydro*-1,2-*dioxo*-4H-*pyrrolo*[3,2,1-ij]*quinoline* (1,7-*Trimethyleneisatin*) **3-*Thiosemicarbazone*.**—Equimolar quantities of the isatin [15] and thiosemicarbazide were refluxed in aqueous ethanol. The *product* was collected, washed with hot water, and crystallised from ethanol, forming orange plates, m. p. 236° (Found: C, 55·4; H, 4·4; S, 12·2. $C_{12}H_{12}N_4OS$ requires C, 55·4; H, 4·6; S, 12·3%).

5-Fluoro-1-*methylisatin* 3-*Thiosemicarbazone*.—Equimolar quantities of 1-sodio-5-fluoro isatin [16] and methyl iodide were refluxed in ethanol for 48 hr. The mixture was filtered and extracted with benzene. Acidification with concentrated hydrochloric acid of a 2N-sodium hydroxide extract of the benzene solution gave 5-fluoro-1-methylisatin as pale red needles, m. p. 151°. The *thiosemicarbazone*, crystallised from ethanol, had m. p. 260° (Found: C, 47·7; H, 3·6; S, 12·4. $C_{10}H_9FN_4OS$ requires C, 47·6; H, 3·6; S, 12·7%).

1-Ethyl-5-fluoroisatin 3-*thiosemicarbazone* was prepared similarly. 1-Ethyl-5-fluoroisatin formed red needles, m. p. 131°, and its *thiosemicarbazone* orange needles, m. p. 228° (Found: C, 49·5; H, 4·0; S, 12·2. $C_{11}H_{11}FN_4OS$ requires C, 49·6; H, 4·1; S, 12·0%).

7-Ethylisatin 3-*thiosemicarbazone* was obtained as orange plates, m. p. 257° (Found: C, 53·4; H, 5·0; S, 12·9. $C_{11}H_{12}N_4OS$ requires C, 53·2; H, 4·8; S, 12·8%).

5-Thiocarbamoylindole.—A solution of 5-cyanoindole (0·1 mole, obtained by the action of cuprous cyanide on 5-bromoindole [17] in quinoline) in 30% (w/v) ammoniacal ethanol (20 c.c.) was saturated with hydrogen sulphide and left for 2 days. The ethanol was removed under reduced pressure and the residual *amide* crystallised several times from hot water, giving white needles, m. p. 162° (Found: C, 61·3; H, 4·4; N, 15·7; S, 18·4. $C_9H_8N_2S$ requires C, 61·4; H, 4·6; N, 15·9; S, 18·2%).

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47. *Aromatic Reactivity. Part XIII.*[1] *Effects of Methyl and t-Butyl Groups in Aromatic Detritiation.*

By C. Eaborn and R. Taylor.

We have measured the rates of detritiation of tritiobenzene and *o*-, *m*-, and *p*-tritio-toluene and -t-butylbenzene in one or more of the following media: aqueous sulphuric acid, acetic acid containing aqueous sulphuric acid, trifluoroacetic acid containing aqueous perchloric acid, and trifluoroacetic acid containing aqueous sulphuric acid.

The spread of rates changes markedly as the medium is varied, probably increasing as the solvating power of the media decreases. The methyl group activates the *para*-position more or less than the t-butyl group, depending on the medium, but it activates the *meta*-position less than the t-butyl group in all cases. The results are discussed in terms of hyperconjugation and solvation influences on the effects of alkyl groups in aromatic substitution.

The accuracy of some earlier reports on preparation of *m*-bromo-t-butylbenzene is questioned.

Previous studies of aromatic hydrogen-exchange reactions of alkylbenzenes have been reviewed by Lauer, Matsen, and Stedman.[2,3] We now report measurements of the rates of detritiation of monotritiated benzene, toluene, and t-butylbenzene by aqueous sulphuric acid, alone or in acetic or trifluoroacetic acid, and by aqueous perchloric acid in trifluoroacetic acid.

Results

The results are listed in the Table. As we have shown,[4] when sulphuric acid is present in the reaction medium for aromatic hydrogen-exchange reactions, the extent of sulphonation must be assessed if accurate results are to be obtained, and the Table lists the observed first-order rate constants, $k_{obs.}$, in sec.$^{-1}$, the first-order rate constants, $k_{sulph.}$, separately measured for sulphonation or estimated by reasonable assumptions specified in footnotes to the Table, and the corrected first-order rate constants, $k_{ex.} = (k_{obs.} - k_{sulph.})$, for the exchange reaction, along with the rate factor, f, denoting the rate of exchange relative to that of [$^3H_1$]benzene. Little error would be introduced by neglecting sulphonation for benzene, *p*-tritiotoluene, and *p*-tritio-t-butylbenzene, but sulphonation is a serious competitor for the *meta*-alkylbenzenes (since the exchange is taking place at the least reactive position of the ring), and accounts for almost half of the observed rate for *m*-tritiotoluene in the trifluoroacetic acid–water–sulphuric acid medium used. Further, in this medium, sulphonation both removes an appreciable proportion of the sulphuric acid present and produces a significant amount of water, and this leads in the case of *m*-tritiotoluene to a fall-off in the integrated rate constant during a run, so that the value of $k_{obs.}$ must be obtained by extrapolation to zero reaction (cf. ref. 5). (With *m*-tritio-t-butylbenzene no fall-off is detected because of the higher $k_{ex.}/k_{sulph.}$ ratio.) Values of $k_{ex.}$ and f for the *meta*-compounds in this medium are thus less reliable than in the other media, but we have no reason to believe that they are more than 10% in error. Exchange in trifluoroacetic acid containing perchloric acid seems free from interfering side-reactions (see Experimental section). It should be stressed that any uncertainties introduced into values of f by sulphonation, or, in the case of the *para*-compounds by the large difference in rate between them and benzene, are not such as to affect the main features of the activation pattern as they are discussed below. In particular, the reactivities of *p*-tritio-toluene and -t-butylbenzene relative to one another are free from significant error.

Since the medium clearly exerts a major influence on the rate factors we cannot compare our results directly with those of previous workers. Our values of f_m^{Me} appear rather large

[1] Part XII, Eaborn and Pande, *J.*, 1961, 297.
[2] Lauer, Matsen, and Stedman, *J. Amer. Chem. Soc.*, 1958, **80**, 6433.
[3] Lauer, Matsen, and Stedman, *J. Amer. Chem. Soc.*, 1958, **80**, 6437.
[4] Eaborn and Taylor, *J.*, 1960, 3301.
[5] Dallinga, Verrijn-Stuart, Smit, and Mackor, *Z. Elektrochem.*, 1957, **61**, 1019.

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Detritiation of X·C_6H_4·^{3}H *compounds in various media at 25°.*

X	71·34 wt.-% H_2SO_4		AcOH–H_2O–H_2SO_4 [a] (26·0)–(34·0)–(40·0)			
	$10^7k_{ex.}$	f	$10^7k_{obs.}$	$10^7k_{sulph.}$	$10^7k_{ex.}$	f
H	—	1	9·32	0·3 [b]	9·0	1
m-Me	—	5·0 [c]	63·4	18·6	44·8	5·0
m-Bu^t	—	—	95·8	12 [d]	84	9·3
o-Me	—	250 [e]	2763	18·6	2744	305
o-Bu^t	—	170 [e]	—	—	—	—
p-Me	1042	250 [c]	2835	18·6	2816	313
p-Bu^t	748	180	2079	12 [d]	2067	230

X	CF_3·CO_2H–H_2O–H_2SO_4 [a] (95·31)–(2·21)–(2·48)				CF_3·CO_2H–H_2O–$HClO_4$ [a] (92·04)–(5·45)–(2·51)	
	$10^7k_{obs.}$	$10^7k_{sulph.}$	$10^7k_{ex.}$	f	$10^7k_{ex.}$	f
H	3·74	<0·15	3·6	1	14·3	1
m-Me	59	26	33	9·2	103	7·2
m-Bu^t	131	17	114	32	339	23·7
o-Me	1974	26	1948	541	4720	330
o-Bu^t	—	—	—	—	5620	393
p-Me	2552	26	2526	702	4480	313
p-Bu^t	3125	17	3108	863	5530	387

[a] The composition of the medium is given (in parentheses) as mole-percentages. For the AcOH–H_2O–H_2SO_4 medium the composition is approximate, and the exact composition is specified in the Experimental section. [b] The rate of sulphonation was too low for measurement, and a value of 1/60 of that for toluene has been assumed. A value of 1/33 applies in aqueous sulphuric acid (cf. Eaborn and Taylor, *J.*, 1960, 1480), and *ca.* 1/150 in some CF_3·CO_2H–H_2O–H_2SO_4 media we have used. [c] Ref. 4. [d] The value of $k_{sulph.}$ is assumed to be 2/3 of that for toluene; this ratio applies in CF_3·CO_2H–H_2O–H_2SO_4. [e] From unpublished results by Mr. R. Baker for a slightly different medium.

when compared with results for deuteration in trifluoroacetic acid [2] ($f_p^{Me} = 420$; $f_m^{Me} = 4$) or for de-deuteration in trifluoroacetic acid containing sulphuric acid [6] ($f_p^{Me} = 350$; $f_m^{Me} = 3·2$). However, the value of f_p^{Me} for the deuteration is subject to a rather large error,[2] estimated to be not more than ±25%, and a value of 5·1, calculated from figures for *p*-xylene in this medium,[2] may be more accurate. Again, the value of f_m^{Me} for the de-deuteration in trifluoroacetic–sulphuric acid was obtained, not by direct comparison of *p*-deuterotoluene and deuterobenzene in one medium, but from an extrapolation based on a dependence of rate on acidity function,[6] while with *m*-deuterotoluene, sulphonation (which, from our experience with somewhat similar media, we believe must have been extensive) was admitted to have caused difficulties, which were not defined. Stock and H. C. Brown [7] have recently shown that, for a large variety of electrophilic aromatic substitutions for which reliable partial rate factors are available, the value of the ratio $(\log f_p^{Me})/(\log f_m^{Me})$ lies between 3·18 and 4·72. Our figures give values of 3·43 (H_2O–H_2SO_4), 3·57 (AcOH–H_2O–H_2SO_4), 2·95 (CF_3·CO_2H–H_2O–H_2SO_4), and 2·91 (CF_3·CO_2H–H_2O–$HClO_4$) for this ratio; the data for deuteration in trifluoroacetic acid give a ratio of 3·60 if f_m^{Me} is taken as 5·1 (but a ratio of 5·04 if f_m^{Me} is taken as 3·2—see above).

The ratio $(\log f_p^{But})/(\log f_m^{But})$ has the values 2·44 (AcOH–H_2O–H_2SO_4), 1·95 (CF_3·CO_2H–H_2O–H_2SO_4), and 1·88 (CF_3·CO_2H–H_2O–$HClO_4$). For a range of electrophilic aromatic substitutions for which data were previously available [8] the ratio lay between 2·27 and 3·82.

Discussion

The main features of our results which require detailed discussion are as follows: (i) The spread of rates varies markedly with the medium. (ii) The activating influence of *p*-methyl and *p*-t-butyl groups can follow either the Baker–Nathan order, Me > Bu^t, or the inductive order, Bu^t > Me, depending on the medium. (For deuteration in trifluoroacetic acid [2] and for de-deuteration in trifluoroacetic–sulphuric acid,[6] the effects of the two groups were identical within experimental error.) Reversal of the order on

[6] Mackor, Smit, and Van der Waals, *Trans. Faraday Soc.*, 1957, **53**, 1309.
[7] Stock and Brown, *J. Amer. Chem. Soc.*, 1959, **81**, 3323.
[8] Brown and Stock, *J. Amer. Chem. Soc.*, 1959, **81**, 5621.

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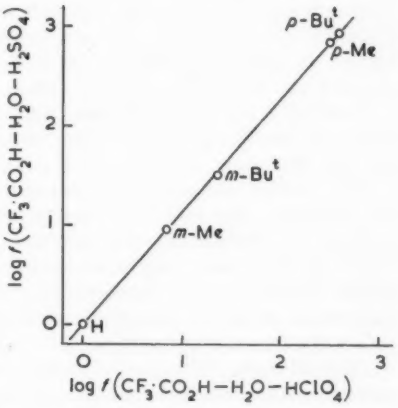
changing the medium has not, so far as we are aware, been observed previously either for ring substitutions or for side-chain reactions which involve rate-determining formation of a carbonium-ion centre adjacent to the ring (though such a dependence has been observed for *meta*-alkyl groups in some reactions of the latter type [9,10]). The only electrophilic aromatic substitution for which an inductive order has previously been reported is nitration in acetic acid containing 10% of water.[11] (iii) For *meta*-substituents the activation order in all the media is clearly $Bu^t > Me$. This order operates in all of the relatively few electrophilic aromatic substitutions for which it has been measured.[8]

We cannot interpret completely the variation in the spread of rates and in the detailed pattern of rate factors as the medium is changed within the range we have used, because so many factors vary together. We can, however, indicate what results we should expect if one property of the medium could be changed independently of the others. These would be as follows: (*a*) If the concentration of the catalysing acidic species could be increased while the solvating power of the medium were kept constant, the rates would increase but the rate factors would remain constant. (Approximation to this state of affairs is probably realised in aqueous sulphuric acid over a small range of acid concentration; cf. ref. 4). (*b*) If the nature of the acidic species could be changed while the solvating power of the medium remained constant, then as the acidity of the catalysing species decreased (and the rates also decreased) so the partial rate factors would increase, because the less electrophilic acidic species would be more selective between the different aromatic compounds (or, in other words, the π-electrons of the ring would be more involved in forming the Ar–HA bond, and the electron-deficiency on the ring in the transition state would be greater). But a linear free-energy relation could be expected between the effects of the substituents in the two media. Change from $CF_3{\cdot}CO_2H{-}H_2O{-}HClO_4$ to $CF_3{\cdot}CO_2H{-}H_2O{-}H_2SO_4$, at the compositions specified in the Table, may approximate to this state of affairs; the rate factors are larger in the latter medium, but a linear free-energy relation exists between the rate factors in the two media (see Figure). (*c*) If the nature of the acidic species could be kept constant while the solvating power of the medium were decreased, the spread of rates would increase. (As the excess of positive charge on the ring in the transition state is less effectively stabilized by solvation, so stabilization of the charge by electron-release from the substituents will increase in importance.) A linear free-energy relation might not hold between the substituent effects in the two media, since (i) the electrical effects of the substituents may be modified internally by specific solvent effects (cf. ref. 9), (ii) polar influences which operate through the medium will be modified as its dielectric constant is changed, and (iii) any steric hindrance to solvation will become less important. (The increase in the spread of rates on changing the medium in the series $H_2O{-}H_2SO_4$, $AcOH{-}H_2O{-}H_2SO_4$, $CF_3{\cdot}CO_2H{-}H_2O{-}HClO_4$, $CF_3{\cdot}CO_2H{-}H_2O{-}H_2SO_4$, probably arises mainly from a fall in the solvating power of the media. The relatively small amount of aqueous sulphuric acid in the trifluoroacetic acid makes the last medium less solvating than the $AcOH{-}H_2O{-}H_2SO_4$ mixture.)



There is considerable controversy about the origin of the activating effects of alkyl

[9] Shiner and Verbanic, *J. Amer. Chem. Soc.*, 1957, **79**, 369.
[10] Schubert, Craven, Minton, and Murphy, *Tetrahedron*, 1959, **5**, 194.
[11] Cohn, Hughes, Jones, and Peeling, *Nature*, 1952, **169**, 291.

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groups in electrophilic aromatic substitution and related reactions.[12-16] The relative effects of methyl and t-butyl groups in electrophilic aromatic substitutions are most often explained by assuming that release of electrons by the inductive effect is in the order $Bu^t > Me$ but that when the C–H bonds of the methyl group are conjugated with a centre of excess positive charge in the ring or in a side chain, hyperconjugation from these bonds can lead to the overall order $Me > Bu^t$ for electron-release.* The activating power for *meta*-groups will then normally be in the order $Bu^t > Me$, but for *para*-groups in the reverse order, though the extent to which hyperconjugation operates may, the argument runs, depend on the electron-demand.[13-15] Thus, in molecular bromination, the pronounced Baker–Nathan order ($f_p^{Me} = 2420$, $f_p^{Bu^t} = 752$, in 85% acetic acid [17]) may result from a large demand for electrons from the alkyl groups to assist polarization and ultimate ionization of the attacking bromine molecule, an electron-demand which shows up in the large f_p^{Me} factor. In nitration in 90% acetic acid,[11] on the other hand, the electron-demand on the substituents is smaller because the highly reactive nitronium ion makes use of the permanent polarization of the substituted ring, and the inductive order of activation results ($f_p^{Me} = 58$, $f_p^{Bu^t} = 75$); [14] the smallness of the electron-demand when compared with that in molecular bromination is reflected in the relatively small value of f_p^{Me}. There are difficulties in this simple picture; for example, in ionic bromination by Br^+ or a related species in aqueous dioxan,[18] the Baker–Nathan order applies, although the electron-demand as measured by f_p^{Me} (*i.e.*, 59) is similar to that in nitration, and it seems that the value of f_p^{Me}, while, by definition, a guide to the overall electron-demand of any reaction, may not necessarily indicate the demand on the time-variable effects of substituents (cf. ref. 19).

Our results within themselves can be nicely explained by use of the concept of hyperconjugation. The greater inductive effect of the t-butyl group results in an inductive order for the *meta*-groups, but hyperconjugation from the methyl group brings the overall effects of the *para*-groups near to equality, and allows the *p*-methyl group to have a greater activating effect than *p*-t-butyl in some media. The change from a Baker–Nathan order to an inductive order as the dielectric constant of the medium is lowered may simply reflect the increase in the direct-field component of the inductive effect.†

The principal objection to relying on C–H hyperconjugation to explain Baker–Nathan orders is that physical measurements, particularly of spectral transition energies, indicate that electron-release by t-butyl groups is about equal to or rather greater than that by the methyl group,[10,20,21] and this has led to suggestions that the Baker–Nathan order in chemical reactions results from steric hindrance by the t-butyl group to solvation of electron-deficient centres in the transition state.[10,20-22] The most compelling single item of evidence is Kosower and Skorcz's observation that methyl and t-butyl groups in the

* For simplicity we neglect consideration of C–C hyperconjugation but it will be appreciated that any observed effect of hyperconjugation must be the difference between C–H hyperconjugation in the methyl, and C–C hyperconjugation in the t-butyl group.

† The medium effect could also be interpreted, less simply, along lines indicated by Shiner and Verbanic [9] in discussing *meta*-alkyl groups.

[12] " Conference on Hyperconjugation " (Co-Chairmen: V. J. Shiner and E. Campaigne), Pergamon Press Ltd., London, 1959; de la Mare, *J. Roy. Inst. Chem.*, 1959, **83**, 634.
[13] Berliner, *Tetrahedron*, 1959, **5**, 202; Berliner and Chen, *J. Amer. Chem. Soc.*, 1958, **80**, 343.
[14] Berliner and Berliner, *J. Amer. Chem. Soc.*, 1954, **76**, 6179.
[15] Robertson, de la Mare, and Swedlund, *J.*, 1953, 782; de la Mare and Robertson, *J.*, 1948, 100; de la Mare, *J.*, 1949, 2871.
[16] Burawoy and Spinner, *J.*, 1954, 3752; 1955, 2085; Spinner, *J.*, 1956, 1590.
[17] Brown and Stock, *J. Amer. Chem. Soc.*, 1957, **79**, 1421.
[18] de la Mare and Harvey, *J.*, (*a*) 1956, 36; (*b*) 1957, 131.
[19] Yukawa, *Bull. Chem. Soc. Japan*, 1959, **32**, 971; Bekhum, Verkade, and Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.
[20] Schubert and Sweeney, *J. Org. Chem.*, 1956, **21**, 119.
[21] Kosower and Skorcz, *J. Amer. Chem. Soc.*, 1960, **82**, 2195.
[22] Clement and Naghizadeh, *J. Amer. Chem. Soc.*, 1959, **81**, 3154.

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4-position have identical effects on the position of the charge-transfer band of 1-methylpyridinium iodides in chloroform.[21] The transition involved is to a state in which the pyridinium ring is essentially uncharged from a ground state in which the nitrogen atom carries a unit positive charge; if C–H hyperconjugation operated, the 4-methyl group would be expected to stabilize this ground state relative to the excited state markedly more than the 4-t-butyl group does, and thus increase the transition energy to a greater extent. (The electron-demand, as measured by the effect of substituents on the transition energy, is very large.) Kosower and Skorcz suggest, as the simplest interpretation of their results, that the electrical effects of alkyl groups are the same and largely depend on the nature of the bond by which they are attached to a given molecule. They further suggest that any deviations from equality of effect, as in chemical reactions, must be explained in other terms, such as steric hindrance to solvation.

In view of the markedly greater activation of the *meta*-position by a t-butyl than by a methyl group in detritiation, as in some other electrophilic reactions, it is unsatisfactory when considering chemical reactivities to regard these groups as having similar electron-releasing properties. To explain our results in terms of steric hindrance to solvation, excluding hyperconjugation from consideration, we should have to assume that the inherent electron-release is clearly in the order $Bu^t > Me$, and that there is negligible steric hindrance to solvation by the *m*- but considerable hindrance by the *p*-t-butyl group. The change in the activation order *p*-Me > *p*-Bu^t to *p*-Me < *p*-Bu^t could then follow as the medium is changed in the direction of decreasing solvating power.* We are not satisfied with this interpretation, partly because the ratio f_o^{Me}/f_p^{Me} is very similar to the ratio f_o^{But}/f_p^{But}, both in trifluoroacetic acid containing sulphuric acid and in aqueous sulphuric acid.[23] If steric hindrance to solvation were as important as it would have to be to explain the large reduction in the relative activation by t-butyl and methyl groups on changing from the *meta*- to the *para*-position, then the latter ratio would be expected to be markedly smaller than the former, since the *o*-t-butyl group, in addition to hindering solvent approach to the ring carbon to which it is attached, should also directly hinder solvation at the reaction centre, near which a large proportion of the excess of positive charge must lie in the transition state.

It seems to us most likely that both hyperconjugation and steric effects operate to determine the effects of *p*-methyl and *p*-t-butyl groups in detritiation. Certainly we feel that hyperconjugation must be invoked in interpreting the influence of alkyl groups on reaction rates, in spite of the difficulty of reconciling this with the influence of the groups on spectral transition energies. One source of difference between effects of substituents on reaction rates and on transition energies is that in a reaction nuclei can move to minimise the free energy at every stage of the progress from reactants to transition state, but the positions of the nuclei cannot change in the time of a spectral transition.† If a transition occurs from a ground state in which hyperconjugation would not be expected, to an excited state in which it would, bond lengths and bond angles cannot adjust to those which are most appropriate for operation of hyperconjugation, and this will act as a restriction on the ease of the electron migrations involved, even though these are not themselves forbidden by the Franck–Condon principle. Conversely, if hyperconjugation is present in the ground state, as would be expected in the case of alkylpyridinium methiodides, then the nuclear positions cannot readjust to conform with disappearance of hyperconjugation in the excited state, and the hyperconjugation is to some extent frozen into the excited state,

* Nothing of significance emerges from attempts to attribute the observed variations to a particular group by analysis of various log *f* ratios. For example, if the steric effect of the *p*-t-butyl group were the only important variant, the ratio $(\log f_p^{But})/(\log f_m^{But})$ would be expected to vary more than $(\log f_p^{Me})/(\log f_m^{Me})$, while the reverse should be true if the hyperconjugative effect of the *p*-methyl group were the only important variant. In fact both ratios vary to much the same extent as the medium is changed.

† The effect of this on solvation has frequently been discussed (see, *e.g.*, refs. 20 and 21).

[23] Baker and Eaborn, unpublished work.

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and its existence in the ground state will thus be hidden. The apparent discordance between effects of alkyl groups in reaction rates and spectral transitions may in part originate in this freezing. The energy involved in the freezing will be small,[24] but the differences between methyl and t-butyl groups which we seek to explain, are themselves small.

Experimental

m-*Bromo-t-butylbenzene.*—Bromine (48 g., 0·3 mole) was added dropwise during 2 hr. to a stirred, refluxing solution of *p*-t-butylacetanilide [25] (53 g., 0·27 mole) in glacial acetic acid (500 ml.). The mixture was refluxed for 6 hr. more and set aside for 18 hr. It was then added to water, and the suspension was decolorised with sodium hydrogen sulphite. The solid was filtered off, washed with water, and recrystallised from aqueous ethanol to give 2-bromo-4-t-butylacetanilide (68·5 g., 91·5%), m. p. 159·5°.

de la Mare and Harvey report m. p. 158° for 2-bromo-4-t-butylacetanilide.[18b] Previous workers have reported 153°,[26] 138·5°,[27] and 138°,[28] and it seems that they were actually dealing with a mixture of the 2-bromo-derivative with unchanged *p*-t-butylacetanilide. Thus on deacetylation and deamination of their product, Cadogan, Hey, and Williams [28] obtained t-butylbenzene as well as *m*-bromo-t-butylbenzene, and assumed that the former product arose from a removal of the bromine atom *ortho* to the diazonium group; from our 4-amino-2-bromo-t-butylbenzene we obtained no t-butylbenzene. We made a few mixtures of *p*-t-butylacetanilide and its 2-bromo-derivative and found them to melt fairly sharply between 135° and 155°.

The 2-bromo-4-t-butylacetanilide was converted into 2-bromo-4-t-butylaniline,[26] b. p. 151°/17 mm., and this was deaminated to give *m*-bromo-t-butylbenzene [28] (89%), b. p. 113°/23·5 mm.

Preparation of Tritiated Compounds.—The preparations of some of the tritiated aromatic compounds have been described; [4] the three tritiated t-butylbenzenes (all *ca.* 5 mc./g.) and *o*-tritiotoluene (*ca.* 5 mc./g.) were made similarly from the aryl bromides. The activities given are maximum values, which may be up to five times too large (cf. ref. 4).

Reaction Media.—" Reagent Grade " acetic acid (May and Baker Ltd.) was purified by Orton and Bradfield's method [29] and fractionally distilled, to give material of m. p. 15·00° calculated [30] to contain 0·8% of water. This acid (631 g.) was mixed with 86·74 wt.-% aqueous sulphuric acid (4828 g.) to give the stock mixture A. For kinetic work 50 ml. portions of this acid were mixed with 10 ml. of 99·2% acetic acid (see below). (The composition of the resulting medium is completely specified by the description we have given of its preparation; we did not measure the density of the medium A, and to calculate the *approximate* molar composition given in the Table we have assumed volume additivity on mixing acetic acid and aqueous sulphuric acid in preparing medium A.)

Anhydrous trifluoroacetic acid was prepared by fractionally distilling the Eastman " White Label " acid (1000 g.) from sulphuric acid (50 g.). The fraction of b. p. 71°/755 mm. was found by titration against alkali to be 100·0% pure. For the kinetics, either (i) the acid (169·51 g.) was mixed with 97·60 wt.-% aqueous sulphuric acid (3·89 g.) and water (0·53 g.) (to give a medium of molar composition, $CF_3{\cdot}CO_2H$, 95·31; H_2O, 2·21; H_2SO_4, 2·48%), or (ii) the acid (194·40 g.) was mixed with 72·02 wt.-% aqueous perchloric acid (6·48 g.) (to give a medium of molar composition, $CF_3{\cdot}CO_2H$, 92·04; H_2O, 5·45; $HClO_4$, 2·51%).

Exchange-rate Measurements.—The general procedures have been described.[4,31]

For reactions in $CH_3{\cdot}CO_2H$–H_2O–H_2SO_4, 50 ml. of medium A (see above) was added (a pipette drainage time of 2½ min. being necessary for reproducibility) to 10 ml. of a solution of the tritiated aromatic compound (*ca.* 1 ml./500 ml.) in 99·2% acetic acid in a tube of 62—63 ml.

[24] Mulliken, *Tetrahedron*, 1959, **6**, 68.
[25] Carpenter, Easter, and Wood, *J. Org. Chem.*, 1951, **16**, 608
[26] Gelzer, *Ber.*, 1888, **21**, 2944.
[27] Crawford and Stewart, *J.*, 1952, 4443.
[28] Cadogan, Hey, and Williams, *J.*, 1954, 3352.
[29] Orton and Bradfield, *J.*, 1927, 963.
[30] de Visser, *Rec. Trav. chim.*, 1893, **12**, 101.
[31] Eaborn and Taylor, *J.*, 1960, 1480.

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capacity. (With a larger vapour space first-order rate coefficients were not satisfactorily constant during a run.) The tube was closed with a Teflon-sleeved standard-taper stopper and placed in a thermostat at 25·0°. Five such tubes were used for each run. Subsequent procedure was as previously described,[4] toluene being used for the extractions. (Initially benzene and t-butylbenzene were used for extraction in reactions involving [$^3H_1$]benzene and [*x*-^{3}H]-t-butylbenzene, but it was later found that use of toluene gave the same results.) Sometimes the extract was slightly yellow, and it was then decolorised with a small amount of activated charcoal; when the extraction solvent was the same as the compound under study, distillation was sometimes used, with identical results.

For runs in trifluoroacetic acid containing sulphuric acid or perchloric acid, a weighed amount (*ca.* 0·1 ml.) of the tritiated aromatic compound was dissolved in a weighed amount (*ca.* 5·5 ml.) of the medium described above. Aliquot parts (1 ml.) were pipetted into drawn-out glass tubes of *ca.* 1·2 ml. capacity, and the tubes were sealed and placed in the thermostat together. The residue of the solution was then weighed so that the weight per aliquot part was known. On removal from the thermostat each tube was broken under 10 ml. of toluene and 100 ml. of 3% aqueous sodium hydroxide. Subsequent procedure was as before,[4] except that, since the mole-ratio of aromatic compound to solvent was larger than in the other media, it could not be assumed that a negligible amount of tritium would remain in the aromatic compound at equilibrium. It was assumed that in benzene all six positions were available for the tritium at equilibrium, and that in runs on *m*-tritiotoluene, and *m*-tritio-t-butylbenzene five positions were available, but that for the other tritiated toluenes and t-butylbenzenes only three positions were available (since tritiation of the *meta*-positions will not be appreciable in ten times the half-life of the detritiation). The error in neglecting isotope effects on the equilibrium is insignificant.

The method is exemplified by the following run involving [$^3H_1$]benzene in $CF_3{\cdot}CO_2H$–H_2O–$HClO_4$ of the composition specified above. Five 1 ml. portions were taken from a solution of 0·0645 g. of [$^3H_1$]benzene in 7·4306 g. of the medium, and the residue weighed 0·192 g., so that there was *ca.* 0·0126 g. of [$^3H_1$]benzene in each of the reaction tubes. Separate measurement showed that this amount of [$^3H_1$]benzene dissolved in 10 ml. of toluene gave a deflection of 228 mm. On the assumption that one position of trifluoroacetic acid, one of perchloric acid, two of water, and six of benzene are equally available for tritium, the benzene hydrogen atoms represent 6·5% of the total available, and at equilibrium the titriated benzene in each sample will give rise to a deflection, D_∞, of 7·3 mm. for each 4·365 g. of the toluene extract (this being the weight used for each activity measurement). The first-order rate coefficient, $k_{obs.}$, is given by $tk_{obs.} = 2{\cdot}303 \log [(D_0 - D_\infty)/(D_t - D_\infty)]$, where D_0 is the deflection (for 4·365 g. of extract) at an arbitrary zero time and D_t the deflection at time t.

Time (hr.)	0	35·75	86·80	155·50	182·0
D_t (mm.)	92·8	78·4	62·1	46·7	40·7
$10^7k_{obs.}$ (sec.$^{-1}$)	—	14·3	14·3	14·3	14·3

The following run illustrates the effect of sulphonation on the $CF_3{\cdot}CO_2H$–H_2O–H_2SO_4 medium. [The value of D_∞ used (4 mm.) is an approximation derived by reducing the value (7 mm.) which would result after 10 half-lives of the exchange alone, by 40% to allow for concurrent sulphonation (see below).] The deflection, D_t, refers to 4·40 g. of extract.

Time (hr.)	0	9·10	21·70	43·40	72·90
D_t (mm.)	194	161	126	90·5	62·0
$10^7k_{obs.}$ (sec.$^{-1}$)	—	57·8	56·7	50·6	45·4

A value of 59×10^{-7} sec.$^{-1}$ for $k_{obs.}$ was derived by extrapolation of the log $(D_t - D_\infty)$–t plot to zero time.

The following run refers to sulphonation of α-tritiated toluene in the same medium as the preceding run. In this case $D_\infty = 0$.

Time (hr.)	0	12·10	34·50	61·00	115·8
D_t (mm.)	157	141	118	100	75
$10^7k_{sulph.}$ (sec.$^{-1}$)	—	24·9	23·0	20·6	17·7

By extrapolation, $k_{sulph.}$ at zero time $= 26 \times 10^{-7}$ sec.$^{-1}$.

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*Rates of Sulphonation.**—Sulphonation of toluene was studied by measuring the loss of α-tritiated toluene as previously described.[31]

Sulphonation of t-butylbenzene was studied by using n-heptane in place of toluene in the extraction process and measuring the optical density, E, of the extract at **247**, **252**, **258**, and **264** mμ. Since the sulphonic acid is removed in the extraction process, the optical densities give a direct measure of the residual concentration of t-butylbenzene, provided no absorbing impurities are present, and the first-order rate constant, $k_{\text{sulph.}}$, is given by $tk_{\text{sulph.}} = 2{\cdot}303 \log (E_0/E_t)$. The following results refer to *t*-butylbenzene (*ca.* 0·18 g.) in $CF_3{\cdot}CO_2H$–H_2O–H_2SO_4 (*ca.* 7·5 g.), figures for only two-wavelengths being quoted:

Time (hr.)	0	116·0	135·8	233·0	305·0
E (247 mμ)	0·267	0·150	0·147	0·116	0·104
E (258 mμ)	0·485	0·276	0·268	0·208	0·190
10^7k (247 mμ) (sec.$^{-1}$)	—	13·8	11·8	9·9	8·6
10^7k (258 mμ) (sec.$^{-1}$)	—	13·5	12·1	10·1	8·6

Extrapolation of the log E_t–t plot to zero time for all four wavelengths gave, on averaging, a value of 17×10^{-7} sec.$^{-1}$ for the initial rate.

With benzene, the same procedure was followed, wavelengths of **243**, **248·7**, **254·5**, and **261** mμ being used.

With t-butylbenzene in the $CH_3{\cdot}CO_2H$–H_2O–H_2SO_4 medium, formation of a yellow colour, some of which persisted into the n-heptane, prevented measurement of the sulphonation rate.

Absence of Side Reactions in Trifluoroacetic acid–Water–Perchloric Acid.—When α-tritiated toluene was used under the conditions of the detritiation of the ring-tritiated toluene in the $CF_3{\cdot}CO_2H$–H_2O–$HClO_4$ medium used, loss of activity was negligible (first-order rate constant $<1 \times 10^{-7}$ sec.$^{-1}$ for $k_{\text{obs.}}$ in the case of [3-$^3H_1$]toluene). This means that (i) no oxidation of the methyl group occurs, and (ii) no other reaction occurs to give either alkali-soluble products, or alkali-insoluble products which influence the tritium measurement. (A substance such as perchloryltoluene, for example, would probably act as an apparent scintillation-quencher relative to toluene.)

Sometimes in longer runs the reaction mixture developed a colour, but this disappeared when the mixture was added to aqueous alkali, and we believe it arises from traces of impurity. First-order rate coefficients were most satisfactorily constant during a run, and mean rate constants could be duplicated to within $\pm 1\%$.

Of the media we have used for detritiation, we believe the $CF_3{\cdot}CO_2H$–H_2O–$HClO_4$ mixture to be most free from troublesome side-reactions.

We thank the Chemical Society for a grant from the Research Fund, the Royal Society for loan of apparatus from the Government Grant in Aid, and the Department of Scientific and Industrial Research for financial assistance.

THE UNIVERSITY, LEICESTER. [*Received, June 16th*, 1960.]

* The media in which we reported $10^6k_{\text{sulph.}}$ values for toluene of 955, 18·8, and 2·58 sec.$^{-1}$ had the following respective compositions (mole percentages in parentheses): $CF_3{\cdot}CO_2H$ (83·40)–H_2O (1·98)–H_2SO_4 (14·62); $CF_3{\cdot}CO_2H$ (85·08)–H_2O (6·42)–H_2SO_4 (8·50); $CF_3{\cdot}CO_2H$ (95·31)–H_2O (2·21)–H_2SO_4 (2·48). The slightly different values given before [31] were calculated in the belief that 99·7% trifluoroacetic acid was used, whereas it was later found to be 100·0%.

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48. *Triterpenoids. Part XXV.* The Constitutions of Limonin and Related Bitter Principles.*

By D. H. R. Barton, S. K. Pradhan, S. Sternhell, and J. F. Templeton.

Extensive investigations on the constitution of the citrus bitter principle, limonin, are reported. By a series of stepwise reactions all the oxygen functions have been in turn inter-related, one of the more important processes used being autoxidation of the anion from the ketone group of limonin which affords the derived diosphenol. By summation of the work reported here with that of others the constitution of limonin has been deduced.[1]

The congeneric bitter principles nomilin and obacunone have been investigated by a study of the commonly derived obacunoic acid. The constitutions which we proposed earlier have received support.

Limonin is the characteristic bitter principle of citrus species and occurs in all parts of the plant. It was first isolated by Bernay in 1841.[2] Limonin represents one of the few remaining classical problems of plant structural chemistry. The literature on this subject has been detailed in a recent paper by Melera, Schaffner, Arigoni, and Jeger [3] and we shall cite in the present paper only those references especially pertinent to our own work.

Our investigations on the constitution of limonin were initiated in Glasgow in 1956 and have been continued to the present time. From the outset we collaborated with Professor J. Monteath Robertson, F.R.S., in an *X*-ray investigation which eventually (see below) made an important contribution to the problem.

Chemical work on the constitution of limonin has also been in progress in Zürich in the laboratories of Professor O. Jeger and Dr. D. Arigoni and at Urbana, Illinois, under the direction of Professor E. J. Corey. During the last three years there has been an exchange of information and free discussion of the problem, and the conclusions reached on the chemical side, summarised in a recent joint communication,[1] represent a collaborative effort. We express here our appreciation of this friendly international exchange. The present paper summarises the experimental work of the Glasgow–Imperial College group and the conclusions that could be drawn from it, with, of course, reference to the *X*-ray work at Glasgow [4] and to other chemical investigations where relevant.

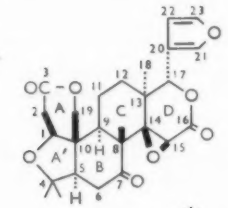
The constitution and stereochemistry of limonin, $C_{26}H_{30}O_8$, can be represented [1,4] as in (I). From the biogenetic point of view the compound is a tetracyclic triterpenoid of the euphol (II) type [5] from which four carbon atoms at the end of the side chain have been removed and carbon atoms 20—23 then converted into a furan ring. Ring A of the triterpenoid skeleton has been oxidatively cleaved between $C_{(3)}$ and $C_{(4)}$ and the 3-carboxyl group thus formed oxidatively cyclised on to $C_{(19)}$. There is excellent precedent for a $C_{(3)}$—$C_{(4)}$ biogenetic cleavage of the triterpenoid skeleton in the recently divulged structures of dammarenolic [6] (III) and nyctanthic acid [6,7] (IV). The constitution of limonin also requires an oxidative cleavage of the Bayer–Villiger type upon a 16-ketone in the skeleton of (II) to give the ring-D lactone. Finally one methyl group must be moved from $C_{(14)}$ to $C_{(8)}$. It is of interest that oxidation of dihydrobutyrospermyl acetate (V) by chromic

* Part XXIV, *J.*, 1958, 2239.

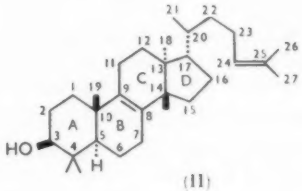
[1] Cf. Arigoni, Barton, Corey, and Jeger, and their collaborators, *Experientia*, 1960, **16**, 41.
[2] Bernay, *Annalen*, 1841, **40**, 317.
[3] Melera, Schaffner, Arigoni, and Jeger, *Helv. Chim. Acta*, 1957, **40**, 1420.
[4] Arnott, Davie, Robertson, Sim, and Watson, *Experientia*, 1960, **16**, 49.
[5] Barton, McGhie, Pradhan, and Knight, *Chem. and Ind.*, 1954, 1325; *J.*, 1955, 876; Arigoni, Viterbo, Dünnenberger, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1954, **37**, 2306; and references there cited.
[6] Arigoni, Barton, Bernasconi, Djerassi, Mills, and Wolff, *Proc. Chem. Soc.*, 1959, 306; *J.*, 1960, 1900.
[7] Whitham, *Proc. Chem. Soc.*, 1959, 271; *J.*, 1960, 2016.

acid furnishes the compound [8] (VI) which has a 7-ketone group, a 14,15-ethylenic linkage, and a β-methyl group moved from $C_{(14)}$ to $C_{(8)}$. It is attractive to suppose that an equivalent mechanism operates in the plant in the biogenesis of limonin. The numbering and lettering systems in limonin (I) follow directly from these biogenetic considerations and are the same as in other tetracyclic triterpenoids.[9]

The absolute configuration of limonin, expected from the biogenetic arguments developed above, has been confirmed [1] by rotatory dispersion curves,[10] kindly measured by Professor W. Klyne (Postgraduate Medical School, London).



(I)



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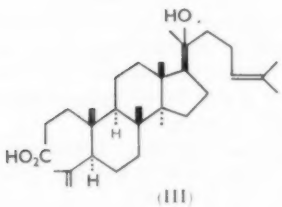

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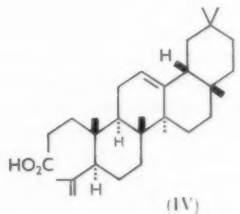

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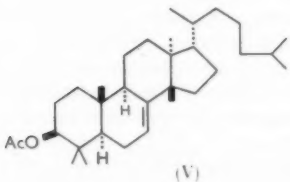

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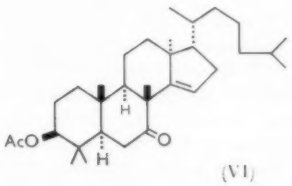

(VI)

Work published either before, or during, our own investigations had shown [1,3] that limonin contains two δ-lactone rings, which can be opened reversibly with alkali, a β-substituted furan residue, a ketonic oxygen present in a six-membered (or larger) ring, and two ethereal oxygen cycles. Hydrogenation of limonin gives tetrahydrolimonin, $C_{26}H_{34}O_8$, and hexahydrolimoninic acid, $C_{26}H_{36}O_8$. The furan ring is saturated in both compounds and the acid is formed by hydrogenolysis of one of the lactone rings. There is good evidence [1,3] that this lactone cleavage is caused by having the alkyl oxygen of the lactone in allylic relation to the furan ring. An exactly comparable situation is found in columbin.[11] Hexahydrolimoninic acid is abnormally strong,[12] a fact which is conveniently explained by attaching one of the ethereal oxygen atoms in the α-position. The partial formula (VII) is thus established.[3]

[8] Lawrie, Hamilton, Spring, and Watson, *J.*, 1956, 3272.
[9] Jones and Halsall, "Fortschritte der Chemie Organische Naturstoffe," Springer-Verlag, Vienna, 1955, Vol. XII, p. 44.
[10] Djerassi, *Bull. Soc. chim. France*, 1957, 741; "Optical Rotatory Dispersion," McGraw-Hill Book Co. Inc., New York, 1960.
[11] Barton and Elad, *J.*, 1956, 2085.
[12] Emerson, *J. Amer. Chem. Soc.*, 1952, **74**, 688.

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The ketone group of limonin can be reduced stereospecifically by the Ponndorff–Meerwein procedure [13] to give the axial alcohol limonol (VIII; R = OH, R′ = H). On the other hand, reduction with borohydride or with sodium amalgam gives the equatorial epilimonol (VIII; R = H; R′ = OH). We have converted epilimonol into its chloroacetate and thence into the iodoacetate (VIII; R = H, R′ = O·CO·CH_2I). It is the latter compound which was used in the *X*-ray work of Robertson and his colleagues.[4] Convenient procedures for the preparation of cholesterol chloroacetate and iodoacetate are also reported in the Experimental section.

Treatment of limonin with hydriodic acid gives first, deoxylimonin,[14] $C_{26}H_{30}O_7$ (IX), and then citrolin,[12,14] $C_{26}H_{28}O_6$. Further reference to these compounds is made below.

The molecular formula of limonin, when coupled with knowledge of the functional groups, requires that the molecule be bicarbocylic. Since drastic degradation [15] of limonin affords 1,2,5-trimethylnaphthalene one can tentatively, and (as it turned out) correctly, assume that the two carbocycles are both six-membered.

We now develop our own arguments in support of the constitution (I). The formation of the αβ-unsaturated lactone deoxylimonin by the action of hydriodic acid on limonin suggests the presence of a 1,2-epoxide.[16] Conjugation of this epoxide with the ring-D lactone carbonyl group was proposed by Professor O. Jeger [17] in a lecture in Glasgow in 1957 in order to explain the conversion of limonol into merolimonol [3] and has since been thoroughly confirmed.[1] In agreement we found that treatment of tetrahydrolimonin (X) with hydrochloric–acetic acid mixture under controlled conditions gave isotetrahydrolimonin, an enolised α-keto-lactone (XI; R = H), characterised as its acetate (XI; R = Ac). The presence of the enolic system, established by a ferric reaction and by spectroscopic data, was confirmed by ozonolysis followed by mild hydrolysis, which afforded oxalic acid.

Treatment of tetrahydrolimonin with hydriodic acid under controlled conditions gave deoxytetrahydrolimonin [as (IX)], also prepared by selective hydrogenation of deoxylimonin (IX). Deoxytetrahydrolimonin was, as expected, stable to acid under the conditions specified above. Treatment of either tetrahydrolimonin or deoxytetrahydrolimonin with hydriodic acid in acetic acid–acetic anhydride at room temperature served to open the tetrahydrofuran ring to give an iodo-acetate (XII). No other change in the molecule was produced (see below), indicating that the second ethereal oxygen was probably not present as a 1,2- or 1,3-epoxide.

The action of hydrochloric acid–acetic acid on hexahydrolimoninic acid (XIII) gave a neutral isomer containing (from the infrared spectrum) a γ-lactone ring. This product is formulated as (XIV) and, in agreement, oxidation with pyridine–chromium trioxide afforded an α-keto-lactone (XV) which could *not* be made to enolise. One must conclude from this that the original isomerisation of (XIII) has placed a new carbon–carbon bond at $C_{(14)}$ in accordance with the formula (XIV). Our own work does not prove that the migrating group is methyl: this is, however, shown conclusively by work carried out at Zürich and Urbana.[1]

When hexahydrolimoninic acid (XIII) was treated with hydriodic acid in acetic acid–acetic anhydride at room temperature it also afforded a γ-lactone (XVI), the tetrahydrofuran ring being opened at the same time. On mild treatment with alkali this product (XVI) gave the γ-lactone (XIV), whilst on reduction with zinc dust it afforded the deiodo-compound (XVII). Oxidation of the latter furnished a non-enolisable α-keto-lactone (XVIII) comparable with the compound (XV) described above.

The relationship between the ketone group of limonin and the lactone ring D was

[13] Chandler and Kefford, *Austral. J. Sci.*, 1951, **14**, 24.
[14] Geissman and Tulagin, *J. Org. Chem.*, 1946, **11**, 760.
[15] Koller and Czerny, *Monatsh.*, 1936, **67**, 248; see also Brachvogel, *Arch. Pharm.*, 1952, **285**, 57.
[16] Cf. Barton, Miller, and Young, *J.*, 1951, 2598.
[17] Jeger, Chem. Soc. Terpene Symposium, Glasgow, July, 1957.

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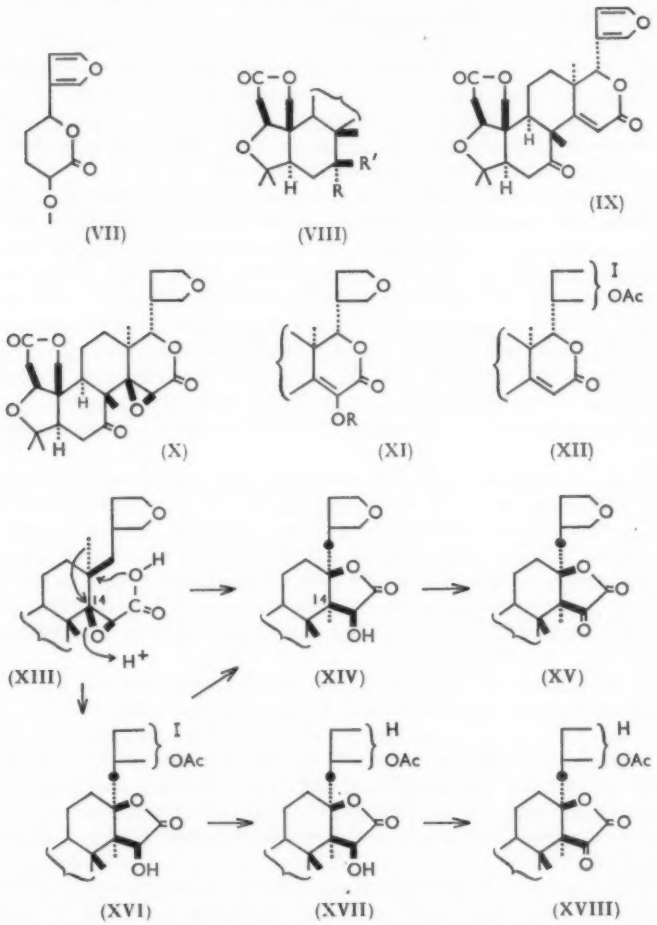
disclosed by the following experiments (see also ref. 1). Treatment of deoxylimonin (IX) under lactone-titration conditions gave a non-conjugated carboxylic acid, $C_{26}H_{32}O_8$, which still retained the two lactone residues but no longer responded to spectroscopic or chemical tests for the ketone group. Deoxylimonin oxime is stable under the same conditions of alkalinity, so that it must be attack by hydroxide ion upon the ketone group which initiates the reaction. All these facts are consistent with a reaction course indicated



in (XIX; arrows) to give (XX) as the structure of the acid, now conveniently designated as deoxylimonic acid. Similarly deoxytetrahydrolimonin (as IX) gave deoxytetrahydrolimonic acid (XXI). This acid was also obtained under the same alkaline conditions from the iodo-acetate (XII) with reclosure of the tetrahydrofuran ring as well as by hydrogenation of deoxylimonic acid.

The further reactions of deoxytetrahydrolimonic acid have confirmed the structure assigned. It reacted with one mole of chlorine to give an adduct [(XXII) or an equivalent] which was too unstable to be isolated. Heating *in vacuo* afforded a mixture of two crystalline diene-acids, both characterised as their methyl esters. The major product

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had a broad absorption band at 255 mμ and a low ε value (7800) in agreement with a *cisoid* diene structure (XXIII). It gave formaldehyde on ozonolysis and had three vinyl-type protons in its nuclear magnetic resonance spectrum, two ($\tau = 4{\cdot}60$ and $4{\cdot}38$) indicative of an exocyclic methylene group (or an equivalent structure), and one ($\tau = 3{\cdot}97$) consistent with the presence of a vinyl hydrogen α to a lactone grouping (as in ring D). The acid (XXIII) was further characterised as the epoxide (XXIV) which showed the spectrum of a normal αβ-unsaturated lactone comparable with that of deoxylimonin. The minor product obtained by heating the adduct (XXII) was a *transoid* diene lactone (XXV) as shown by its ultraviolet spectrum [$\lambda_{max.}$ 230 and 284 mμ (ε 6300 and 16,400 respectively)]. These two diene lactones not only confirm the relationship of the 7-ketone group of limonin to the ring-D lactone group, but also show the presence of an 8-methyl group and a 9-hydrogen atom.

The environment of the 7-ketone group of limonin was defined in a simple manner which may well have more extensive application.[18] Limonin in dry t-butyl alcohol containing potassium t-butoxide was rapidly autoxidised to the diosphenol (XXVI; R = H) characterised as its acetate (XXVI; R = Ac). Analogous diosphenols, (XXVII) and (XXVIII) respectively, were obtained from deoxylimonin (IX) and tetrahydrolimonin (X). These compounds show that limonin contains the system (–$\overset{\beta}{C}$H·$\overset{\alpha}{C}$H$_2$·CO). The position of the ultraviolet maximum near 280 mμ further indicated [19] that there was very probably only one hydrogen atom β with respect to the ketone group of limonin, as in the partial formula given below.

These diosphenol formulations were further confirmed by the ozonolysis of the derivative (XXVIII) from tetrahydrolimonin. This gave in good yield a nor-acid (XXIX) characterised as its methyl ester. Treatment of this acid with aqueous alkali afforded formaldehyde, a reaction comparable with those recorded in the chemistry of icterogenin [20] and iresin.[21] The presence of the grouping (–CO·O·CH$_2$·C·C=O) in the nor-acid (XXIX) is thus established. In its infrared spectrum the methyl ester of acid (XXIX) showed a carbonyl band at 1760 cm.$^{-1}$: this cannot be due to either of the lactones A and D, for the trisodium salt (two lactones opened and the carboxyl group neutralised) still showed a carbonyl band near 1750 cm.$^{-1}$; it must be ascribed to the new ketone function produced in the ozonolysis. This enhanced frequency is consistent with a cyclopentanone with an α-ethereal substituent.[22]

Limonilic acid,[12] $C_{26}H_{30}O_9$, was first obtained [14] by oxidation of limonin in alkaline solution with potassium permanganate, but it is more readily prepared in essentially quantitative yield by treatment of an alkaline solution of limonin with hypoiodite.[12] Limonilic acid is to be formulated as (XXX) on the basis of the following considerations.[1] Emerson had shown [12] that hexahydrolimoninic acid (XIII) gave a dicarboxylic acid (XXXI) on oxidation with hypoiodite. The lactone ring modified in the reaction was, therefore, lactone A and not that (lactone D) opened by hydrogenolysis. In confirmation, reduction of limonilic acid with hydriodic acid in the usual way gave a deoxylimonilic acid (as IX) with an αβ-unsaturated ring-D lactone group comparable with that in deoxylimonin itself (IX). We found that, contrary to earlier observations,[12] methyl limonilate contained no hydroxyl group (infrared spectrum). Bearing these facts in mind, and having regard to the stoicheiometry of the reaction,[12] we see that formation of

[18] See, *e.g.*, Bailey, Elks, and Barton, *Proc. Chem. Soc.*, 1960, 214; Davis and Weedon, *ibid.*, p. 182; Barton and (J.) Templeton, unpublished work.

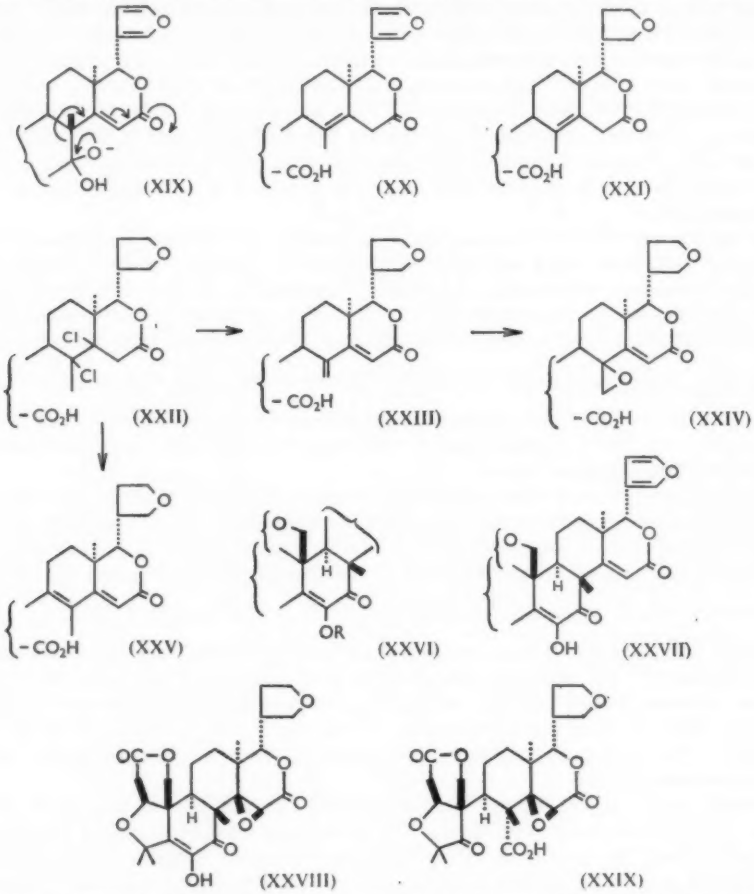
[19] See Fieser and Fieser, "Natural Products Related to Phenanthrene," 3rd edn., Reinhold Publ. Corpn., New York, 1949, p. 195.

[20] Barton and de Mayo, *J.*, 1954, 887.

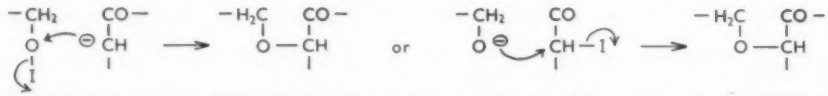
[21] Djerassi and Burstein, *J. Amer. Chem. Soc.*, 1958, **80**, 2593, and earlier papers there cited.

[22] Cf. Cookson and Dandegaonker, *J.*, 1955, 352; Baumgartner and Tamm, *Helv. Chim. Acta*, 1955, **38**, 441.

limonilic acid must involve conversion of the alkyl-oxygen of lactone A, already characterised (see above) as of the type $-CH_2{\cdot}O{\cdot}CO-$, into either an aldehyde or an ether grouping. Now the ketone group of limonin is also profoundly modified as a result of the limonilic



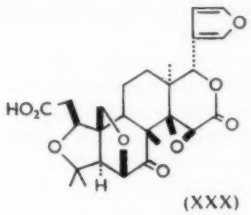
acid change. Thus it no longer gives an oxime or undergoes the diosphenol reaction (see above). Also it has displaced ultraviolet and infrared bands relative to those of limonin itself. These facts are consistent with the presence of an axially oriented ether substituent in the α-position (6β) with respect to the ketone grouping. There is no evidence for the presence of an aldehyde function in limonilic acid. We concluded, therefore, that the conversion of limonin into limonilic acid involved a change of the type



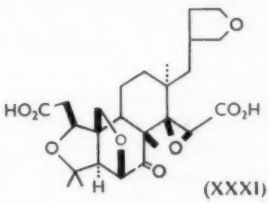
These views were confirmed by the important observation announced by Professor O. Jeger and his colleagues at the Glasgow Terpene Symposium [17] that reduction of limonilic acid with aluminium amalgam gave back limonin. The other properties of limonilic acid were likewise interpreted by Professor Jeger [17] as in the text above.

XUM

The genesis of limonilic acid from limonin represents a new procedure for the formation of an ethereal linkage facilitated, no doubt, by a specially favourable conformational situation.



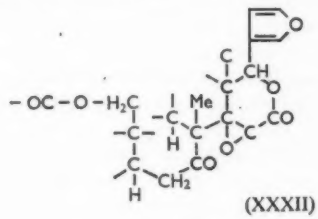
(XXX)



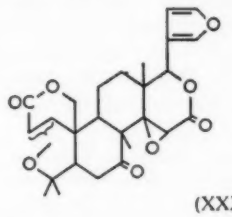
(XXXI)

The work of our group outlined above, coupled with earlier published work on limonin, makes it possible to write without ambiguity the partial structure (XXXII). If we accept a triterpenoid type of biogenesis [1] and have regard to the formation of acetone in high yield on fusion with potassium hydroxide [12] and to the formation of naphthalenic products [3,15] on dehydrogenation then one can write (XXXIII) as a plausible formula for limonin (see ref. 1). This was the position in September, 1959, when Professor Monteath Robertson was able to state from the *X*-ray evidence (see ref. 1) that limonin was either (I) or (XXXIV). The latter formula is, of course, incompatible with much chemical evidence and therefore formula (I) stands. In addition, the *X*-ray work provides the complete stereochemistry of the molecule.

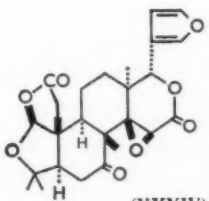
The formulæ (I) and (IX) for limonin and deoxylimonin respectively permit the formulation of citrolin as in (XXXV). The earlier work of Emerson [12] had established that citrolin contained an αβ-unsaturated ketone function as well as an αβ-unsaturated lactone and a furan ring. A study of the hydrogenation of citrolin [12] appeared to show that these were the only unsaturated groupings present. We noted, however, that the ultraviolet and infrared spectra of citrolin were in better accord with the presence of *two* αβ-unsaturated lactone groups. This was confirmed by the selective hydrogenation of citrolin (under conditions which do not attack the unsaturation of ring D) to give a dihydrocitrolin (XXXVI). In this compound the presence of a saturated δ-lactone ring could be



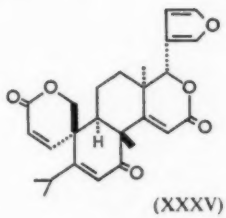
(XXXII)



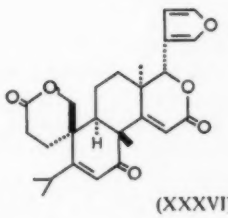
(XXXIII)



(XXXIV)



(XXXV)



(XXXVI)

seen directly in the infrared spectra and indirectly by differential ultraviolet spectroscopy with respect to deoxylimonin (IX). The nuclear magnetic resonance spectrum of citrolin confirmed the presence of 4 *C*-methyl groups.

Other aspects of limonin chemistry which can be interpreted in terms of formula (I), but to which we have made no experimental contribution, have already been discussed in the joint communication [1] and, therefore, do not merit repetition here.

The two minor bitter principles of citrus species are [23] nomilin, $C_{28}H_{34}O_9$, and obacunone, $C_{26}H_{30}O_7$. They have recently been investigated further by Dean and Geissman.[24] Both compounds contain two lactone rings, one of which can be opened reversibly and the other irreversibly, a furan ring, a somewhat unreactive ketone group, and an ethereal ring. Nomilin is a β-acetoxy-lactone which, on treatment with a suitable hot tertiary amine, is converted into the αβ-unsaturated lactone obacunone with elimination of acetic acid. Upon consideration of these and other published facts discussed in more detail below, and having regard to a probable biogenetic relation to limonin, one of us (D. H. R. B.) proposed [1] the formulæ (XXXVII) and (XXXVIII) for nomilin and obacunone respectively. The work that we summarise in the sequel, whilst not providing a complete proof of the correctness of these structures, is nevertheless in full accord with them and confirms many of the relationships of the functional groups. In addition we have resolved certain anomalies in the earlier work [24] which were in apparent disagreement with our proposed formulæ.

Both nomilin and obacunone on mild treatment [23,24] with alkali afford obacunoic acid, $C_{26}H_{32}O_8$ (XXXIX; R = H), in which the ring-A lactone has been opened irreversibly as expected of a seven-membered ring. Obacunoic acid has two active hydrogen atoms, in keeping with the presence of a normal alcoholic hydroxyl group, a feature about which there was some confusion earlier.[24] Methyl obacunoate [24] (XXXIX; R = Me) likewise showed a hydroxyl band of normal type in the infrared spectrum. The nuclear magnetic resonance spectrum of this ester confirmed the presence of four normal *C*-methyl groups (τ = 8·88, 8·97, 9·008, and 9·043), one *C*-methyl group (τ = 8·618) of the type at $C_{(13)}$ in limonin (that is, close to the furan ring), and a *cis*-β-substituted acrylic ester [*A*–*B* quartet at τ 4·24 and 4·49 (α-H) and at τ 3·798 and 4·08 (β-H); J_{AB} = 13·4 c./sec.; see ref. 25). In addition, two α-hydrogen (τ = 2·506) and one β-hydrogen atom (τ = 3·658) attached to a furan ring [26] could be clearly characterised. One proton with a τ value of 4·63 indicated >CH·O– at position 17, a feature seen in the nuclear magnetic resonance spectra of limonin and its derivatives.

On hydrogenation in acetic acid over palladised charcoal, obacunoic acid consumed 3·74 mols. of hydrogen. Methyl obacunoate behaved similarly (3·86 mols. uptake) and gave a crystalline acid ester (XL) through hydrogenolysis of the D-ring lactone just as in limonin (see above). The consumption of hydrogen in our hands is one mol. less than that observed earlier.[24] We conclude, therefore, that obacunone and nomilin are bicarbocyclic, like limonin, not monocarbocyclic as proposed [24] earlier on the basis of the hydrogenation evidence.

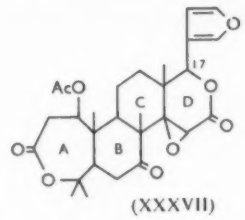
Obacunoic acid behaved like limonin on reduction with chromous chloride [1] and afforded a crystalline deoxyobacunoic acid. This contained an αβ-unsaturated lactone ring regarded as δ because of its infrared frequency. A similar conclusion as to the size of the reversibly opened (D-ring) lactone can be reached from the infrared spectra of all obacunoic acid derivatives (for details see Experimental section). Deoxyobacunoic acid behaved like deoxylimonin (see above) in that mild treatment with base gave a product (XLI) which, on spectroscopic evidence, lacked the αβ-unsaturated lactone ring. It did not crystallise but was clearly an analogue of deoxylimonic acid (XX).

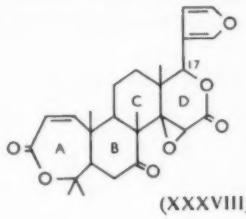
Another analogy between limonin and obacunoic acid could be seen in the following transformation. Treatment of the methyl ester acid (XL) with dioxan–hydrochloric acid under the conditions needed to transform hexahydrolimoninic acid (XIII) into its rearranged isomer (XIV) gave an acidic product which, from its infrared spectrum, was

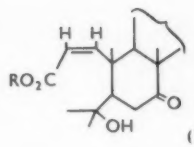
[23] Emerson, *J. Amer. Chem. Soc.*, 1948, **70**, 545; 1951, **73**, 2621; and references there cited.
[24] Dean and Geissman, *J. Org. Chem.*, 1958, **23**, 596.
[25] Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959.
[26] Corey, Slomp, Sukh Dev, Tobinaga, and Glazier, *J. Amer. Chem. Soc.*, 1958, **80**, 1204.

XUM

also a γ-lactone (band at 1785 cm.$^{-1}$). In addition this substance showed αβ-unsaturated ketone absorption in the ultraviolet region, but with an infrared carbonyl frequency which was abnormally low (1630 cm.$^{-1}$). The same anomalously low carbonyl frequency is found in compound (XIV) (1686 cm.$^{-1}$) and must be due to hydrogen bonding with the


(XXXVII)


(XXXVIII)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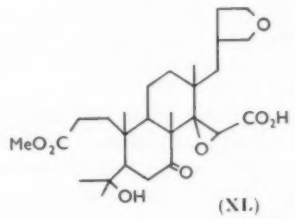
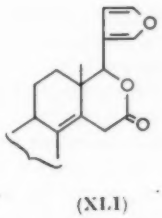
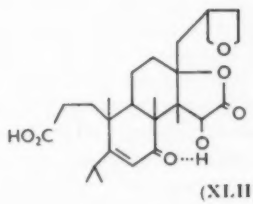
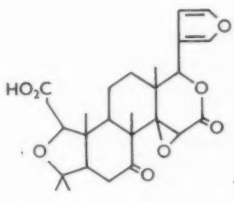
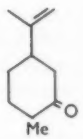
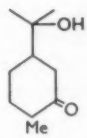

(XL)

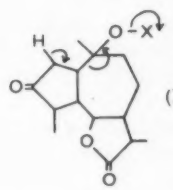

(XLI)

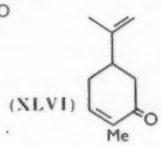

(XLII)

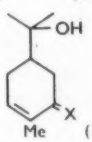

(XLIII)

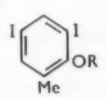

(XLIV)


(XLV)


(XLIX)


(XLVI)


(XLVII)


(XLVIII)

15-hydroxyl group. In (XIV) the λ-lactone frequency is also somewhat exalted (at 1789 cm.$^{-1}$). The reaction product is, therefore, formulated as (XLII) although it too did not crystallise.

On mild treatment with sodium methoxide, methyl obacunoate was converted into iso-obacunoic acid (XLIII). This substance lacked the αβ-unsaturated acid function of obacunoic acid and also (see below) the hydroxyl group. The facts are nicely explained by formula (XLIII) and, indeed, the formation of such an iso-acid is in full accord with the proposed [1] (see also above) biogenesis of limonin.

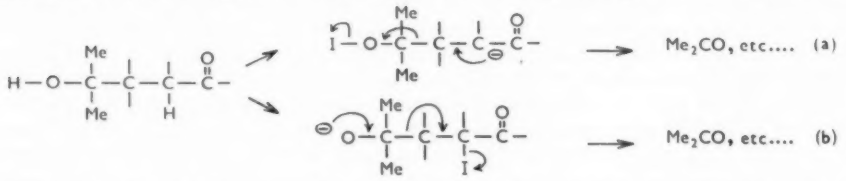
Dean and Geissman [24] made the interesting observation that obacunone gives a positive iodoform test. Under standard conditions [27] the following yields of iodoform were obtained: acetophenone 30, acetonedicarboxylic ester 16, 21, obacunoic acid 15, limonin 0, iso-obacunoic acid 0, cinnamic acid 0, crotonic acid 0%. These results show that it is the hydroxyisopropyl grouping of obacunoic acid which is responsible for the test. There are two obvious mechanisms which would explain this.

Route (a) appears the more probable, but we do not have any decisive experiment to

[27] Fieser, "Experiments in Organic Chemistry," Heath and Co. Inc., Boston, 1955.

XUM

distinguish between the two. We have shown, however, that model compounds react in the same way. Thus, whilst dihydrocarvone [28] (XLIV) gave no iodoform, its hydrate [29] (XLV) gave 4%. Similarly carvone (XLVI) furnished no iodoform, but its hydrate [30] (XLVII; X = O) gave 6%. From the latter reaction the expected 4,6-di-iodo-*o*-cresol (XLVIII; R = H), characterised as its 3,5-dinitrobenzoate, could be isolated. α-Terpineol (XLVII; X = H_2) afforded no iodoform, but dihydroisophotosantonic lactone [31]



(XLIX; X = H), where an analogous mechanism indicated in (XLIX; X = I; see arrows) can operate, gave 4%. These iodoform experiments, taken as a whole, suggest that obacunoic acid has a hydroxyisopropyl group separated by two carbon atoms from the ketone group as already written into formula (XXXIX).

The environment of the ketone group of obacunoic acid was further defined by autoxidation experiments of the kind described above for limonin and its derivatives. Alkaline autoxidation of obacunoic acid gave a diosphenol, characterised as its acetate, in the manner expected. However, the ε values for these compounds were significantly lower than for compounds of the limonin series, and both the diosphenol and its acetate analysed for one H_2O less than expected. In addition, both compounds were neutral, not acidic. Formulæ which explain these facts are (L), (LI), and (LIII) according to which a normal diosphenol acid (L) is first formed but then rearranges, if only fleetingly, to (LI), collapse of which [(LI); see arrows, or equivalent displacements] gives the diosphenol (LIII; R = H).

Autoxidation of iso-obacunoic acid gave an acidic diosphenol with the normal spectroscopic and chemical properties expected of a structure (LII). However, it did not crystallise.

If all the facts on obacunoic acid are summarised and the interpretations made in the deduction [1] of the limonin structure are repeated then, by assuming also that the ring-A lactone of obacunone is 7-membered, the partial expression (LIV) for obacunone can be derived fairly rigidly.

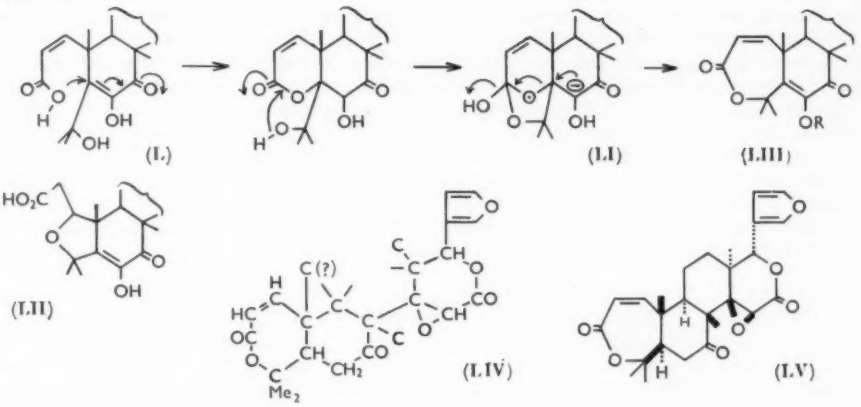
The stereochemistry of obacunone is not defined by the above experiments. However, the change in $[M]_D$ between limonin and epilimonol is almost exactly the same as that between obacunone and α-obacunol, the borohydride reduction product of obacunone,[24] indicating an analogous stereochemical environment. The change in $[M]_D$ from obacunoic acid to deoxyobacunoic acid is not, however, in good agreement with the corresponding change in the limonin series. We assumed that obacunone was related, stereochemically as well as constitutionally, to limonin and was thus (LV). An attempt to inter-relate limonin and obacunone was, therefore, initiated along the following lines.

Limonilic acid (XXX) was transformed by a standard series of reactions [32] into the corresponding methyl ketone (LVI; X = O) which was then converted into the dithioketal [LVI; X = ·S·CH_2·)$_2$]. Preliminary experiments showed that limonilic acid could be reduced back efficiently to limonin by the use of lithium amalgam (for large-scale preparation of this amalgam, see the Experimental section) and that a typical dithioketal

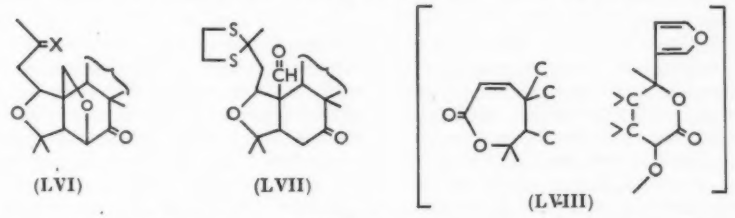
[28] Wallach and Schrader, *Annalen*, 1894, **279**, 377.
[29] Rupe and Liechtenhan, *Ber.*, 1906, **39**, 1124.
[30] Knoevenagel and Samel, *Ber.*, 1906, **39**, 677.
[31] Barton, de Mayo, and Shafiq, *J.*, 1957, 929.
[32] See, *e.g.*, Wolfrom and Brown, *J. Amer. Chem. Soc.*, 1943, **65**, 1516; Barton, Campos-Neves, and Scott, *J.*, 1957, 2698.

XUM

was not reduced by this reagent under the experimental conditions employed. Treatment of the thioketal (LVI) in this way and oxidation of the product with pyridine–chromium trioxide then furnished the keto-aldehyde (LVII). Conversion of the aldehyde group into methyl should afford a derivative of iso-obacunoic acid. So far, however, it has not been possible to reduce the aldehyde group of (LVII) without damaging other functional groups in the molecule. A further report will be presented if we ultimately attain this objective.



After the completion of our experiments there appeared a preliminary communication by Kubota, Kamikawa, Takoroyama, and Matsuura [33] in which independent evidence is



presented for the partial structure (LVIII) for obacunane. All the observations of the Japanese authors are in agreement with our proposed formula (XXXVIII) for this bitter principle.

Experimental

M. p.s were taken on the Kofler block. Ultraviolet absorption spectra are for EtOH solutions unless stated otherwise. Rotations were determined for $CHCl_3$ solutions except where otherwise specified. Infrared spectra were taken for Nujol mulls unless stated to the contrary. Light petroleum refers to the fraction of b. p. 40—60°. Microanalyses were by Mr. J. M. L. Cameron (Glasgow) and Miss J. Cuckney (Imperial College) and their respective associates. Neutral alumina, graded according to the Brockmann scale of activity, was used in chromatography. For general experimental procedures see earlier work.[34]

Nuclear magnetic resonance spectra were kindly determined and interpreted by Drs. L. M. Jackman and J. W. Lown to whom we express our best thanks. The spectra were taken in $CDCl_3$ using a Varian Associates spectrometer model V.4311 at a fixed frequency of 56·445 Mc./sec. Line positions were measured by the conventional side-band technique with a Muirhead Decade oscillator (model D 695-A) and with tetramethylsilane as internal reference. For general information on definition of τ and other symbols see ref. 25.

[33] Kubota, Kamikawa, Tokoroyama, and Matsuura, *Tetrahedron Letters*, 1960, No. 8, p. 1.
[34] Barnes, Barton, Fawcett, and Thomas, *J.*, 1952, 2339.

XUM

Extraction of Limonin (*with* Mr. G. F. PHILLIPS).—The following procedure represents a convenient method for the extraction of limonin. Crushed citrus seeds (3 kg.) and commercial acetone (17 l.) were left at room temperature with occasional stirring for 2—3 weeks. The extract was decanted and filtered. The residual meal was washed with further acetone (1 l.) and processed similarly. The total acetone solution was concentrated to a syrup and then mixed with good stirring with light petroleum (b. p. 60—80°; 2·5 l.). With commercial acetone two layers may be formed, with solid at the interface; with a good grade of acetone the crude limonin is precipitated without separation of the solvent into two layers. The acetone–light petroleum (b. p. 60—80°) mixture was left at room temperature for 1—3 days and then filtered. The solid was twice made into a slurry with ethanol (150 ml.) and filtered each time. The filtrate after the second washing was almost colourless. A solution of crude limonin (suitably 24 g.) in methylene dichloride (250 ml.) was filtered, concentrated to about 100 ml., and treated with propan-2-ol (200 ml.). The solution was concentrated to the first sign of crystallisation and then left for several hours at room temperature. This gave pure limonin (12 g.), m. p. 298°, $[\alpha]_D$ −125° (in acetone), −132°, +36° (in N-ethanolic potassium hydroxide), $\lambda_{max.}$ 207 and 285 mμ (ε 7000 and 38 respectively), $\nu_{max.}$ 3124, 1603, 1505, and 876 (furan), 1755—1760 (δ-lactones) and 1706 (ketone) cm.$^{-1}$.

Various sources of limonin were investigated with the results indicated in the Table. The outstanding advantage of grapefruit seeds will be obvious.

Species and origin of citrus seeds	Limonin isolated (%) Average	Best
Valencia orange (S. Rhodesia)	0·32	0·41
Orange (S. Rhodesia)	0·42	0·54
Lemon (unknown source)	0·08	—
Lime (Jamaica)	0·20	0·21
Grapefruit (Trinidad)	0·66	0·86

Limonin was characterised as the oxime,[23] m. p. 236—239°, $[\alpha]_D$ −115° (*c* 1·00 in acetone), $\lambda_{max.}$ 201 mμ (ε 7200).

Deoxylimonin (with Mr. G. F. PHILLIPS).—Limonin (300 mg.) in "AnalaR" acetic acid (7 ml.) and concentrated aqueous hydriodic acid (5 ml.) was kept at 55° for 4 hr. (optimum time). Dilution with water, extraction into chloroform, and washing with aqueous sodium hydrogen sulphite and then aqueous sodium hydrogen carbonate gave deoxylimonin [14] (30%). Recrystallised from acetone–methanol this had m. p. 331—336°, $[\alpha]_D$ −39° (*c* 1·08), $\lambda_{max.}$ 214 mμ (ε 17,000), $\nu_{max.}$ 1747 (δ-lactone), 1714 (αβ-unsaturated δ-lactone), 1699 (ketone) cm.$^{-1}$, as well as the usual furan bands. Deoxylimonin (100 mg.) in dry pyridine (2 ml.) was treated with hydroxylamine hydrochloride (100 mg.) in ethanol (1·0 ml.) and left for 7 days at room temperature. Recrystallisation of the product from aqueous ethanol gave *deoxylimonin oxime*, m. p. 258—259°, $[\alpha]_D$ +31° (*c* 1·00 in acetone), $\nu_{max.}$ 3300 (OH), 1735 (δ-lactone), 1709 (αβ-unsaturated δ-lactone) and 1626 (C=N) cm.$^{-1}$ (Found: C, 66·45; H, 6·55; N, 3·4. $C_{26}H_{31}NO_7$ requires C, 66·5; H, 6·65; N, 3·0%).

Reduction of deoxylimonin under more vigorous conditions [14] gave citrolin, identical with material obtained in the same way by direct reduction of limonin. Recrystallised from benzene–ether this had m. p. 297—298°, $[\alpha]_D$ −140° (*c* 1·00), $\lambda_{max.}$ 212, 238, and 338 mμ (ε 23,200, 18,300, and 150 respectively), $\nu_{max.}$ 1717 (lactones), and 1667 (αβ-unsaturated ketone) cm.$^{-1}$ as well as the usual furan bands.

Citrolin was also obtained conveniently by the following procedure. Deoxylimonin (716 mg.) in hydrogen bromide in glacial acetic acid (50% w/v; 10 ml.) was refluxed for 40 min. Crystallisation of the neutral product from acetone and from tetrahydrofuran–propan-2-ol gave pure citrolin (392 mg.), identified by m. p., mixed m. p., and infrared spectrum.

Dihydrocitrolin.—Citrolin (71·4 mg.) in dioxan (10 ml.) was hydrogenated over pre-reduced palladised charcoal (10% w/w; 114 mg.) until just over 1 mol. of hydrogen had been absorbed. The neutral product, crystallised from methylene dichloride–propan-2-ol or from acetone–ethanol, gave *dihydrocitrolin* (XXXVI) (50 mg.), m. p. 282—286°, $[\alpha]_D$ −106° (*c* 1·00), $\lambda_{max.}$ 216 mμ (ε 17,200), $\lambda_{shoulder}$ 231—243 mμ (ε 14,700), $\nu_{max.}$ 1756 (δ-lactone), 1712 (αβ-unsaturated δ-lactone), 1667 and 1500 (αβ-unsaturated cyclohexanone) cm.$^{-1}$ (Found: C, 71·4; H, 7·15. $C_{26}H_{30}O_6$ requires C, 71·2; H, 6·9%).

Cholesteryl Iodoacetate.—Cholesterol (100 mg.) in dry dioxan (5 ml.) was treated with chloroacetyl chloride (0·5 ml.) at room temperature overnight. Addition of water gave the

chloroacetate which, after recrystallisation from chloroform–ethanol (80 mg.), had m. p. 156—159°, $[\alpha]_D$ −39° (*c* 1·43). Diels and Stamm [35] give m. p. 162°.

The chloroacetate (100 mg.) and finely powdered potassium iodide (400 mg.) in acetone (8 ml.) were heated under reflux for 3 hr. Crystallisation of the product from chloroform–methanol furnished *cholesteryl iodoacetate* (90 mg.), m. p. 121—123°, $[\alpha]_D$ −22° (*c* 2·06) (Found: C, 62·8; H, 8·05; I, 23·25. $C_{29}H_{47}IO_2$ requires C, 62·8; H, 8·55; I, 22·9%).

Epilimonol Iodoacetate.—Reduction of limonin with potassium borohydride essentially as described by Melera, Schaffner, Arigoni, and Jeger [3] gave epilimonol, m. p. 262—266°, $[\alpha]_D$ +9° (*c* 1·12 in acetone) (Found: C, 66·15; H, 7·05. Calc. for $C_{26}H_{32}O_8$: C, 66·1; H, 6·85%). The derived acetate had m. p. 298—301° (Found: C, 65·55; H, 6·75. Calc. for $C_{28}H_{34}O_9$: C, 65·35; H, 6·65%). The derived *methanesulphonate*, obtained from treating epilimonol (440 mg.) in dry pyridine (14 ml.) with methanesulphonyl chloride (5 ml.) at room temperature overnight, had, after crystallisation from acetone–light petroleum (300 mg.), m. p. 218°, $[\alpha]_D$ −10° (*c* 1·51) (Found: C, 58·85; H, 6·15; S, 5·95. $C_{27}H_{34}O_{10}S$ requires C, 58·9; H, 6·2; S, 5·8%).

Epilimonol (1·5 g.) in dry chloroform (100 ml.) was refluxed with chloroacetyl chloride (35 ml.) in the presence of pyridine (3 drops) for 5½ hr. Careful addition of water and separation of the chloroform layer gave *epilimonol chloroacetate* (1·10 g.), m. p. (from aqueous acetone) 265—268°, $[\alpha]_D$ +16° (*c* 1·44 in acetone) (Found: C, 59·1; H, 6·1. $C_{28}H_{33}ClO_9,H_2O$ requires C, 59·3; H, 6·2%).

Epilimonol chloroacetate (100 mg.) and sodium iodide (1·0 g.) in acetone (20 ml.) were refluxed for 4 hr. Crystallisation of the product from aqueous acetone gave *epilimonol iodoacetate*, m. p. 211—214° decomp., $[\alpha]_D$ +22° (*c* 1·54 in acetone) (Found: I, 19·9. $C_{28}H_{33}IO_9$ requires I, 19·8%).

Limonol Methanesulphonate.—Limonol [3,13] (200 mg.) in dry pyridine (16 ml.) was treated with methanesulphonyl chloride (4 ml.) at 0° and left at 0° for 3 days. Crystallisation of the product from acetone–methanol afforded the *ester* (89 mg.), m. p. 205—210° (decomp.), $[\alpha]_D$ −74° (*c* 1·07 in acetone) (Found: C, 59·1; H, 6·05. $C_{27}H_{34}O_{10}S$ requires C, 58·9; H, 6·2%).

Deoxyepilimonol.—Deoxylimonin in dioxan was reduced with potassium borohydride essentially as for the preparation of epilimonol (see above). Crystallisation of the product from acetone–light petroleum furnished *deoxyepilimonol*, m. p. 300—305°, $[\alpha]_D$ +61° (*c* 0·70 in acetone), $\lambda_{max.}$ 212 mμ (ε 17,300), $\nu_{max.}$ 3390 (OH) and 1730 and 1706 (δ-lactones) cm.$^{-1}$ (Found: C, 68·55; H, 7·1. $C_{26}H_{32}O_7$ requires C, 68·4; H, 7·05%). Treatment of deoxyepilimonol with an excess of methanesulphonyl chloride in pyridine overnight at room temperature afforded the *methanesulphonate*. Recrystallised from acetone–ethanol this had m. p. 245—246° (decomp.), $[\alpha]_D$ +62° (*c* 0·72 in acetone), $\lambda_{max.}$ 213—214 mμ (ε 17,200) (Found: C, 60·75; H, 6·45; S, 6·1. $C_{27}H_{34}O_9S$ requires C, 60·65; H, 6·4; S, 6·0%).

The Diosphenol (XXVIII) *from Tetrahydrolimonin and its Congeners.*—Tetrahydrolimonin (finely powdered; 2·5 g.) suspended in t-butyl alcoholic N-potassium t-butoxide (200 ml.) was shaken with oxygen in a standard hydrogenation apparatus for 1—2 hr. (uptake of 1 mol. of oxygen). Water (200 ml.) was added and then 6N-hydrochloric acid (50 ml.). The solution was extracted with chloroform (3 × 100 ml.), and the extracts were washed with saturated aqueous sodium hydrogen carbonate (2 × 25 ml.) and then water (100 ml.). The chloroform solution was then shaken with aqueous 4N-sodium hydroxide (2 × 25 ml.). Acidification of this extract with aqueous 6N-hydrochloric acid gave a white precipitate which was extracted in chloroform (3 × 50 ml.) again. The chloroform solutions were washed with water (2 × 50 ml.), and the solvent was removed (70—90% of acidic material). Crystallisation from methylene dichloride–ethanol gave the *diosphenol* (XXVIII) (60%), m. p. 157—161°, $[\alpha]_D$ −223° (*c* 1·26 in acetone), $\lambda_{max.}$ 278 mμ (ε 11,000), $\lambda_{max.}$ 336—340 mμ (ε 6300 in 0·1N-sodium hydroxide; reversible shift), $\nu_{max.}$ 3484 (OH), 1754 and 1739 (δ-lactones), and 1695 and 1653 (diosphenol cm.$^{-1}$ (Found: C, 63·05; H, 7·25. $C_{26}H_{32}O_9,C_2H_6O$ requires C, 62·9; H, 7·15%). The compound gave an immediate ferric chloride test.

In a similar way limonin (1·0 g.) was converted into the corresponding *diosphenol* (XXVI; R = H) (470 mg.). Recrystallised from acetone–ethanol this had m. p. 273—288°, $[\alpha]_D$ −200° (*c* 1·00 in acetone), $\lambda_{max.}$ 207 and 278 mμ (ε 7900 and 10,100), shifted reversibly in alkali to $\lambda_{max.}$ 336 mμ (ε 6150), $\nu_{max.}$ 3484 (OH), 1748 and 1736 (δ-lactones), and 1689 and 1661 (diosphenol)

[35] Diels and Stamm, *Ber.*, 1912, **45**, 2228.

cm.$^{-1}$ (Found: C, 64·3; H, 6·1. $C_{26}H_{28}O_9$ requires C, 64·45; H, 5·85%). This diosphenol (200 mg.) was treated with excess of pyridine–acetic anhydride (1 : 1) overnight at room temperature. Crystallisation of the product from methylene dichloride–ethanol furnished the *diosphenol acetate* (XXVI; R = Ac) (184 mg.), m. p. 292—299°, $[\alpha]_D$ −101° (*c* 1·20), $\lambda_{max.}$ 210 and 245 mμ (ε 8800 and 11,000 respectively), $\nu_{max.}$ 1751 and 1739 (δ-lactones and diosphenol acetate), 1695 (αβ-unsaturated ketone), and 1650 (conjugated ethylenic linkage) cm.$^{-1}$ (Found: C, 63·3; H, 6·1; Ac, 8·15. $C_{28}H_{30}O_{10}$ requires C, 63·8; H, 5·7; Ac, 8·75%).

The same autoxidation process converted deoxylimonin (300 mg.) into its *diosphenol* (XXVII). Recrystallised from acetone–ethanol this (175 mg.) had m. p. 310—317°, $[\alpha]_D$ −112° (*c* 0·93 in acetone), $\lambda_{max.}$ 282 mμ (ε 10,400), 335 mμ (ε 5200 in N-ethanolic potassium hydroxide), $\nu_{max.}$ 3480 (OH), 1764 and 1733 (δ-lactones) and 1681 (diosphenol) cm.$^{-1}$ (Found: C, 66·55; H, 6·1. $C_{26}H_{28}O_8$ requires C, 66·65; H, 6·0%). Treatment with pyridine–acetic anhydride overnight at room temperature gave the corresponding *acetate*, m. p. (from acetone–ethanol) 262—264°, $[\alpha]_D$ −74° (*c* 1·53 in acetone), $\lambda_{max.}$ 213—214 and 246 mμ (ε 18,000 and 13,000 respectively), $\nu_{max.}$ 1764, 1733, and 1706 (δ-lactones and acetate), 1684 (αβ-unsaturated ketone), and 1605 (conjugated ethylenic linkage) cm.$^{-1}$ (Found: C, 65·6, 66·05; H, 6·05, 6·25. $C_{28}H_{30}O_9$ requires C, 65·85; H, 5·9%).

Degradation of the Diosphenol (XXVIII) *from Tetrahydrolimonin.*—The diosphenol (500 ml.) in chloroform (50 ml.) was ozonised at −20° until the diosphenol chromophore had been destroyed (20 min.). Water (25 ml.) was added, the chloroform removed on the steam-bath, and heating continued for 15 min. Excess of sodium hydrogen carbonate was added and the solution extracted with chloroform to remove traces (10 mg.) of neutral material. Acidification with 6N-hydrochloric acid and extraction into chloroform afforded the *nor-acid* (XXIX). Recrystallised from methylene dichloride–ethanol, this (75%) had m. p. 208—212° (decomp.), $[\alpha]_D$ −200° (*c* 0·80 in acetone), $\lambda_{max.}$ 296 mμ (ε 37), $\nu_{max.}$ 1760 (exalted cyclopentanone), 1735 and 1725 (δ-lactones and carboxylic acid) cm.$^{-1}$ (Found: C, 61·2; H, 6·35. $C_{25}H_{28}O_{10}$ requires C, 61·45; H, 6·35%). Treatment with an excess of ethereal diazomethane in a little dioxan gave the corresponding *methyl ester*, m. p. (from acetone–light petroleum) 215—221°, $[\alpha]_D$ −190° (*c* 1·56 in acetone), $\nu_{max.}$ 1761 (exalted cyclopentanone), and 1739 and 1727 (δ-lactones and methoxycarbonyl group) cm.$^{-1}$ in $CHCl_3$ (Found: C, 61·4; H, 6·75. $C_{26}H_{30}O_{10}$ requires C, 61·65; H, 6·75%).

The nor-acid (163 mg.) was left in aqueous 4N-sodium hydroxide (3·0 ml.) at room temperature overnight under oxygen-free nitrogen. The solution was acidified with 6N-sulphuric acid (2 ml.) and distilled into aqueous dimedone (2 × theor.). This gave the dimedone–formaldehyde condensation product (13·8 mg., 23%), identified by m. p. and mixed m. p. The appropriate control gave none of this derivative.

The nor-acid (170 mg.) was treated as described above except that the distillate was collected in a solution of 2,4-dinitrophenylhydrazine in methanolic sulphuric acid. Filtration in benzene solution through alumina (grade III) gave formaldehyde 2,4-dinitrophenylhydrazone (17%), identified by m. p., mixed m. p., and ultraviolet absorption spectrum. A control experiment gave none of this derivative.

Limonilic Acid and Its Derivatives.—Limonilic acid was prepared according to Emerson's method.[12] Recrystallised from propan-2-ol–light petroleum it had m. p. 290—292°, $[\alpha]_D$ +104° (*c* 1·92 in acetone). The derived methyl ester (diazomethane–ether), crystallised from the same solvent mixture, had m. p. 231—233°, $[\alpha]_D$ +111° (*c* 1·01 in acetone), $\lambda_{max.}$ 307 mμ (ε 37), $\nu_{max.}$ 1735 and 1715 (δ-lactones and ketone) cm.$^{-1}$. There was no sign of a hydroxyl band in the infrared spectrum.

When epilimonol was treated with iodine and alkali under the conditions used for making limonilic acid [12] it was recovered unchanged in high yield.

Limonilic acid was recovered unchanged after being shaken under oxygen with potassium t-butoxide in t-butyl alcohol as in the preparation of the series of diosphenols (see above).

The rate of alkaline hydrolysis of methyl limonilate was compared with that of other esters in the following way. The methyl ester (0·02 milliequiv.) in dioxan (5 ml.) and aqueous 0·04N-sodium hydroxide (5 ml.) was kept at 25° and the uptake of alkali determined in the usual way by removal of 1 ml. aliquot portions. Preliminary experiments with methyl limonilate showed that the lactone ring was opened essentially instantaneously. Correction was made, therefore, for this by the appropriate adjustment of the concentration of aqueous sodium hydroxide used. The same applies for the hexahydro-derivative of methyl limonilate (which has a free carboxyl group). The times for half-hydrolysis, in parentheses, were: (i) methyl propionate (8·5 min.),

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(ii) methyl isobutyrate (24 min.), (iii) methyl α-methoxy-α-methylpropionate (26 min.), (iv) hexahydro-derivative of methyl limonilate (31 min.), (v) methyl limonilate [approx. as for (iv)].

Isotetrahydrolimonin.—Tetrahydrolimonin (880 mg.) in (3 : 2) acetic acid–concentrated hydrochloric acid (20 ml.) was heated on the steam-bath for 1½ hr. Crystallisation of the product from acetone–ethanol gave *isotetrahydrolimonin*, m. p. 263—266°, $[\alpha]_D$ −102° (*c* 0·96 in acetone), $\lambda_{max.}$ 256 mμ (ε 5300), changing to $\lambda_{max.}$ 290 mμ (ε 4600) on addition of 1 drop of N-ethanolic potassium hydroxide, $\nu_{max.}$ 1740 and 1710 (δ-lactones and ketonic carbonyl group) and 1660 (conjugated ethylenic linkage) cm.$^{-1}$ (Found: C, 65·6; H, 7·55. $C_{26}H_{34}O_8$ requires C, 65·8; H, 7·2%). Treatment with excess of pyridine–acetic anhydride overnight at room temperature afforded *isotetrahydrolimonin acetate*. Recrystallised from aqueous ethanol this had m. p. 192—196°, $[\alpha]_D$ −150° (*c* 1·00 in acetone), $\lambda_{max.}$ 218 mμ (ε 11,000), $\nu_{max.}$ 1745 and 1720 (δ-lactones, enolic acetate and ketonic carbonyl group), and 1630 (conjugated ethylenic linkage) cm.$^{-1}$ (Found: C, 63·0; H, 7·35. $C_{28}H_{36}O_9,H_2O$ requires C, 62·9; H, 7·15%).

Isotetrahydrolimonin (249 mg.) in chloroform (50 ml.) was ozonised at −20° until the absorption at $\lambda_{max.}$ 256 mμ was negligible (25 min.). Water (15 ml.) was added and the chloroform distilled off. The resultant clear aqueous solution was kept on the steam-bath for 30 min. The water was removed *in vacuo* to give the product, which did not crystallise. The crude product was warmed with 0·4N-sodium hydroxide for 20 min. (standard procedure for equivalent determination) and found to give an equiv. of 138 (Calc. for 3 acid groups, 169). The neutralised solution, treated with saturated aqueous calcium nitrate, gave an immediate precipitate of calcium oxalate (80%) identified by crystal form and infrared spectrum.

Deoxylimonic Acid and its Derivatives.—Deoxylimonin (470 mg.) was heated with aqueous 2N-sodium hydroxide (40 ml.) for 1½ hr. on the steam-bath. The clear alkaline solution was acidified with hydrochloric acid and extracted into ether. Crystallisation of the acidic product from propan-2-ol gave *deoxylimonic acid* (260 mg.), m. p. 247—250°, $[\alpha]_D$ −166° (*c* 1·26 in acetone) [Found: C, 66·2; H, 6·55%; equiv. (excess of 4N-aqueous sodium hydroxide on steam-bath for 10 min.; then back-titration to phenolphthalein), 153, 158. $C_{26}H_{32}O_8$ requires C, 66·1; H, 6·85%; equiv. (3 acidic groups), 157]. Limonin showed an equiv. of 234 (theor., 235) under the same conditions. *Methyl deoxylimonate*, prepared with diazomethane in the usual way, had, after crystallisation from propan-2-ol, m. p. 164—167°, $[\alpha]_D$ −154° (*c* 1·25 in acetone), ε = 11,400 at 208 mμ, $\nu_{max.}$ 1720—1755 (δ-lactones and carbomethoxyl) cm.$^{-1}$, no hydroxyl band (Found: C, 66·6; H, 6·85; OMe, 6·15. $C_{27}H_{34}O_8$ requires C, 66·65; H, 7·05; OMe, 6·35%). The ester gave no oxime under the conditions used for the preparation of deoxylimonin oxime (see above). Deoxylimonic acid did not undergo a limonilic-type reaction with alkaline hypoiodite.

Deoxylimonin oxime was treated with alkali under the conditions used (see above) for making deoxylimonic acid but was recovered unchanged (193 mg. from 220 mg.).

Deoxylimonilic Acid and Derivatives.—Limonilic acid (150 mg.) in " AnalaR " acetic acid (3·5 ml.) and concentrated aqueous hydriodic acid (2·5 ml.) was kept at 55° for 4 hr. Crystallisation of the acidic product from propan-2-ol–light petroleum afforded *deoxylimonilic acid* (87 mg.), m. p. 275—278°, $[\alpha]_D$ +47° (*c* 1·56 in acetone) (Found: C, 66·0; H, 6·25. $C_{26}H_{30}O_8$ requires C, 66·35; H, 6·45%). The derived *methyl ester*, prepared with ethereal diazomethane in the usual way, had, after crystallisation from propan-2-ol–light petroleum, m. p. 213—215°, $[\alpha]_D$ +46° (*c* 1·64 in acetone), $\lambda_{max.}$ 213—214 mμ (ε 15,400), broad infrared band at 1700—1730 cm.$^{-1}$ (δ-lactones and carbomethoxyl group) (Found: C, 66·45; H, 6·65; OMe, 6·15. $C_{27}H_{32}O_8$ requires C, 66·9; H, 6·65; OMe, 6·4%).

Deoxylimonilic acid, treated with alkali under the conditions used (see above) for the preparation of deoxylimonic acid, did not go into solution and was recovered unchanged. The acid (100 mg.) was, therefore, refluxed with methanolic 5% potassium hydroxide (10 ml.) for 30 min. The methanol was removed *in vacuo*, excess of aqueous hydrochloric acid added, and the product separated into acidic and neutral (negligible) fractions. Crystallisation of the acidic fraction from propan-2-ol–light petroleum gave back deoxylimonilic acid (62 mg.), identified by m. p., mixed m. p., and ultraviolet absorption spectrum.

Deoxytetrahydrolimonin.—(a) *From tetrahydrolimonin.* Tetrahydrolimonin (100 mg.) in " AnalaR " acetic acid (3·5 ml.) and concentrated aqueous hydriodic (2·5 ml.) was kept at 55° for 3½ hr. Crystallisation of the product from methylene dichloride–ethanol afforded *deoxytetrahydrolimonin*, m. p. 293—297°, $[\alpha]_D$ −88° (*c* 1·30 in $CHCl_3$), $\lambda_{max.}$ 219 mμ (ε 10,800), $\nu_{max.}$ 1752, 1720 (sh) and 1710 (δ-lactones and ketonic carbonyl) cm.$^{-1}$ (Found: C, 68·15; H, 7·4.

$C_{26}H_{34}O_7$ requires C, 68·1; H, 7·45%). On crystallisation from methanol this compound melted at 178—182°.

(b) *From deoxylimonin.* Deoxylimonin (1·0 g.) was dissolved in warm acetic acid (100 ml.) and then hydrogenated over 10% palladised charcoal (1·0 g.) (1 mol. uptake). Crystallisation of the product from methylene dichloride–ethanol afforded deoxytetrahydrolimonin identical with the compound described above.

After treatment with acid as for the preparation of isotetrahydrolimonin (see above) deoxytetrahydrolimonin was recovered unchanged in high yield.

Iodoacetate (XII) *from Ring-cleavage of Deoxytetrahydrolimonin.*—(a) *From tetrahydrolimonin.* Tetrahydrolimonin (367 mg.) was warmed at 55° with a mixture of "AnalaR" acetic acid and concentrated hydriodic acid (10 ml.) for 3½ hr. The neutral product, crystallised from ethanol, gave the *iodoacetate*, m. p. 238—239°, $[\alpha]_D$ −105° (*c* 0·85), −118° (*c* 1·03 in acetone), $\lambda_{max.}$ 219 mμ (ε 12,700), $\nu_{max.}$ 1710 and 1732 (δ-lactones, acetate and ketonic carbonyl) cm.$^{-1}$ (Found: C, 53·8; H, 6·0; Ac, 6·9, 7·3. $C_{28}H_{37}IO_8$ requires C, 53·5; H, 5·9; Ac, 6·85%).

(b) *From deoxytetrahydrolimonin.* Deoxytetrahydrolimonin (260 mg.) in 1 : 4 acetic anhydride–acetic acid (10 ml.) was treated dropwise at room temperature with concentrated hydriodic acid (3 ml.) and left for 16 hr. Crystallisation of the product from ethanol–light petroleum gave the above iodoacetate (40 mg.), identified by m. p., mixed m. p., and ultraviolet and infrared spectra.

Deoxytetrahydrolimonic Acid.—(a) *From deoxytetrahydrolimonin.* Deoxytetrahydrolimonin (150 mg.) was heated on the steam-bath for 2 hr. with aqueous 2N-sodium hydroxide (30 ml.). Acidification with 6N-hydrochloric acid gave *deoxytetrahydrolimonic acid.* Recrystallised from aqueous acetone this had m. p. 276—284°, $[\alpha]_D$ −89° (*c* 1·10 in pyridine), $\lambda_{max.}$ 202 mμ (ε 11,300), $\nu_{max.}$ 1758, 1730, and 1716 (δ-lactones and carbonyl group) cm.$^{-1}$ (Found: C, 65·5; H, 7·8. $C_{26}H_{36}O_8$ requires C, 65·55; H, 7·6%).

(b) *From deoxylimonic acid.* Deoxylimonic acid (572 mg.) was hydrogenated in acetic acid (75 ml.) over 10% palladised charcoal (1·0 g.) (uptake 1 mol.). Crystallisation of the product from aqueous acetone gave deoxytetrahydrolimonic acid, identified by m. p., mixed m. p., and infrared spectrum.

(c) *From the iodoacetate* (XII) *from deoxytetrahydrolimonin.* The iodoacetate (XII) (272 mg.) was shaken with potassium hydroxide (3 g.) in water (20 ml.) until dissolved and then left at room temperature for 19 hr. Acidification with 2N-sulphuric acid gave deoxytetrahydrolimonic acid (184 mg.), identified, after crystallisation from aqueous acetone, in the usual way.

Derivatives of Deoxytetrahydrolimonic Acid.—Deoxytetrahydrolimonic acid (720 mg.) in acetic acid (100 ml.) was treated with chlorine (0·20 mmole) in carbon tetrachloride (28 ml.) and left in the dark at room temperature for 16 hr. The mixed solvent was removed *in vacuo* and the residue heated at 110° for 3 hr. also *in vacuo*. Crystallisation from acetone–ether gave the cisoid *diene-acid* (XXIII) (390 mg.), m. p. 259—269°, $[\alpha]_D$ +231° (*c* 0·80), $\lambda_{max.}$ 255 mμ (ε 7800) in a broad band, $\nu_{max.}$ 1760, 1714, and 1703 (δ-lactones and carboxyl), and 1619 and 1600 (C=C) cm.$^{-1}$ [Found: C, 65·7; H, 7·4%; equiv. (saponification and back-titration), 174. $C_{26}H_{34}O_8$ requires C, 65·8; H, 7·2%; equiv. (3 acidic functions), 160]. The crude material obtained after removal of the mixed solvents but before the heating period (see above) was also examined. It had $\lambda_{max.}$ *ca.* 230 mμ (ε 6000) and a shoulder at *ca.* 250 mμ (ε 4000). Crystalline *cisoid* diene-acid (XXIII) was obtained from this product in poor yield. During the heating period the spectrum slowly changed to that expected for a mixture of *cisoid* and *transoid* (see below) diene-acids. Ethanolic potassium hydroxide or collidine gave similar results to heating but the products were not so clean. On a spectroscopic basis the ratio of *cisoid* to *transoid* isomers was between 2 : 1 and 4 : 1.

The *cisoid* diene-acid (XXIII) was characterised in the following way. The *methyl ester*, prepared with ethereal diazomethane (45 min. at room temperature) had, after crystallisation from acetone–ether, m. p. 200—204°, $[\alpha]_D$ +226° (*c* 1·30), $\lambda_{max.}$ 255 mμ (ε 7700) in a broad band (Found: C, 66·2; H, 7·35. $C_{27}H_{36}O_8$ requires C, 66·35; H, 7·45%). Treatment of the acid (XXIII) (74 mg.) with 80% peracetic acid (2 ml.), previously saturated with sodium acetate, for 16 hr. at 0° gave, after crystallisation of the product from acetone–ether, the *epoxide* (XXIV) (35 mg.), m. p. 243—249°, $[\alpha]_D$ +88° (*c* 0·40), $\lambda_{max.}$ 217—218 mμ (ε 9100), $\nu_{max.}$ 1767, 1715, and 1708 (δ-lactones and carbonyl group) cm.$^{-1}$ (Found: C, 63·85; H, 7·15. $C_{26}H_{34}O_9$ requires C, 63·65; H, 7·0%).

The *cisoid* diene-acid (133 mg.) in chloroform (20 ml.) was ozonised at −20° for 15 min.

(spectroscopic control). Zinc dust (500 mg.) and water (8 ml.) were added and the mixture was distilled. The distillate was treated with excess of aqueous dimedone solution and the chloroform distilled off. After 20 hr. the formaldehyde derivative was filtered off (18·5 mg., 13%) and identified by m. p. and mixed m. p. Under identical conditions pyrethrosin [36] (110 mg.) gave 13·4% of the formaldehyde–dimedone derivative. The appropriate controls were also run.

The mother-liquors from the crystallisation of the *cisoid* diene-acid (see above) were concentrated and left to crystallise. This gave the isomeric transoid *diene-acid* (XXV) (80 mg.), m. p. (from acetone–ether) 260—271°, $[\alpha]_D$ +260° (*c* 1·20 in CH_2Cl_2), $\lambda_{max.}$ 230 and 284 mμ (ε 6300 and 16,400 respectively), $\nu_{max.}$ 1748, 1730, and 1704 (δ-lactones and carbonyl group), and 1594 (C=C) cm.$^{-1}$ (Found: C, 64·75; H, 7·0. $C_{26}H_{34}O_8$,0·5H_2O requires C, 64·6; H, 7·3%). The derived *methyl ester*, prepared as for the *cisoid* ester (see above) and crystallised from acetone–ether, had m. p. 207—212°, $\lambda_{max.}$ 229 and 283 mμ (ε 5400 and 18,600 respectively) (Found: C, 65·1; H, 7·2. $C_{27}H_{36}O_8$,0·5H_2O requires C, 65·7; H, 7·5%).

Isomerisation of Hexahydrolimoninic Acid.—Hexahydrolimoninic acid (500 mg.) in dioxan (6 ml.) and concentrated hydrochloric acid (6 ml.) was heated for 14 hr. on the steam-bath. Crystallisation of the neutral product from methylene dichloride–acetone afforded *isohexahydrolimoninic acid* (XIV), chars at 315°, $[\alpha]_D$ −82° (*c* 0·58), end-absorption only in the ultraviolet region, infrared bands at 3333 (OH), 1789 (γ-lactone), 1755 (δ-lactone), and 1686 (hydrogen-bonded carbonyl) cm.$^{-1}$ (Found: C, 65·4; H, 7·7; active H, 0·22. $C_{26}H_{36}O_8$ requires C, 65·55; H, 7·6; active H, 0·21%).

Isohexahydrolimoninic acid (226 mg.) was left at room temperature for 22 hr. with a ground mixture of chromium trioxide (700 mg.) in pyridine (6 ml.). Water (20 ml.) was added and the excess of oxidant destroyed with sulphur dioxide. The neutral product (181 mg.), recrystallised from methylene dichloride–ethanol or from acetone–ethanol, gave *dehydroisohexahydrolimoninic acid* (XV), m. p. 245—253°, $[\alpha]_D$ −43° (*c* 1·50), no high-intensity ultraviolet absorption, $\nu_{max.}$ 1792 (γ-lactone), 1777 (α-keto-γ-lactone), 1760 (δ-lactone), and 1720 (non-hydrogen-bonded ketonic carbonyl) cm.$^{-1}$ (Found: C, 66·0; H, 7·25. $C_{26}H_{34}O_8$ requires C, 65·8; H, 7·2%).

Iodoacetate (XVI) *from Ring-cleavage of Hexahydrolimoninic Acid.*—Hexahydrolimoninic acid (640 mg.) in " AnalaR " acetic acid (16 ml.), acetic anhydride (4 ml.), and concentrated hydriodic acid (6 ml.) was left at room temperature for 24 hr. Working up gave a neutral product (751 mg.) which, on repeated crystallisation from ethanol, afforded the *iodoacetate* (XVI), m. p. 227—229°, $[\alpha]_D$ −59° (*c* 1·50 in acetone), $\lambda_{max.}$ 255 mμ (ε 500), $\nu_{max.}$ 3220 (OH), 1790 (γ-lactone), 1755 (δ-lactone), 1730 (OAc), and 1677 (hydrogen-bonded ketonic carbon) cm.$^{-1}$ (Found: C, 52·5, 52·5, 52·45; H, 5·95, 6·15, 5·9; I, 21·25; Ac, 6·75. $C_{28}H_{39}IO_9$ requires C, 52·15; H, 6·05; I, 19·65; Ac, 6·65%).

This iodoacetate (500 mg.) in " AnalaR " acetic acid (50 ml,) was heated on the steam-bath with zinc powder (3 g.) for 10 min. with constant shaking. Crystallisation of the product from methylene dichloride–ethanol gave the *γ-lactone acetate* (XVII), m. p. 246—256°, $[\alpha]_D$ −76° (*c* 1·31 in acetone), $\lambda_{max.}$ 290 mμ (ε 26), $\nu_{max.}$ 3300 (OH), 1790 (γ-lactone), 1751 (δ-lactone), 1730 (OAc) and 1683 (hydrogen-bonded ketonic carbonyl) cm.$^{-1}$ (Found: C, 64·3; H, 7·9; Ac, 8·5; active H, 0·18. $C_{28}H_{40}O_9$ requires C, 64·6; H, 7·75; Ac, 8·25; active H, 0·19%).

The iodoacetate (XVI) (200 mg.) was heated on the steam-bath for 30 min. with aqueous N-sodium hydroxide (15 ml.). Crystallisation of the neutral product from methylene dichloride–ethanol furnished isohexahydrolimoninic acid, identified especially by its infrared spectrum.

The γ-lactone acetate (XVII) (290 mg.) in pyridine (5·5 ml.) was slowly added to a ground suspension of chromium trioxide (364 mg.) in pyridine (3 ml.) and left at room temperature overnight. Addition of water, destruction of the excess of oxidant with sulphur dioxide, and extraction in the usual way gave a neutral product (284 mg.) which, recrystallised from methylene dichloride–ethanol and then acetone–ethanol, furnished the *α-keto-γ-lactone* (XVIII), m. p. 235—239°, $[\alpha]_D$ −45° (*c* 1·60 in acetone), $\nu_{max.}$ 1792 (γ-lactone), 1775 (α-keto-γ-lactone), 1750 with shoulder (δ-lactone and acetate) and 1717 (non-hydrogen-bonded ketonic carbonyl) cm.$^{-1}$ (Found: C, 64·7; H, 7·55; Ac, 8·1. $C_{28}H_{38}O_9$ requires C, 64·85; H, 7·4; Ac, 8·3%).

Methyl Norlimonilyl Ketone (LVI; X = O).—Limonilic acid (2·06 g.) in tetrahydrofuran (30 ml.) and oxalyl chloride (5 ml.) was heated under reflux for 1 hr. The mixed solvents were removed *in vacuo* and the residual limoniloyl chloride crystallised from benzene–light petroleum and dried *in vacuo* at 50°. Reliable analytical data were not secured for this compound but it

[36] Barton and de Mayo, *J.*, 1957, 150.

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showed infrared bands at 1791 (acid chloride), 1740 (δ-lactone), and 1722 (cyclohexanone with α-ether group) cm.$^{-1}$ and gave methyl limonilate, identified by m. p. and mixed m. p., (214 mg. from 234 mg. of acid), on dissolution in methanol. The crystalline chloride, in dry tetrahydrofuran (30 ml.), was poured slowly into a solution of diazomethane in dry ether (prepared from 25 g. of *N*-methylnitrosourea) with cooling to 0°. The solution was left at room temperature for 1 hr. and then the ether was removed *in vacuo* at 30—40°. The residue was dissolved in chloroform (25 ml.) and shaken with hydriodic acid (*d* 1·7; 6 ml.) for 5 min. The neutral product in ethanol (30 ml.) was refluxed with aqueous 0·4N-sodium hydroxide (30 ml.) on the steam-bath for 30 min. with gradual removal of the ethanol. After cooling, the aqueous solution was extracted with chloroform (discarded) and then acidified, and the neutral product (1·58 g.) was extracted in benzene. After drying (Na_2SO_4), this extract was filtered through alumina (grade I; 6 g.). Crystallisation from benzene–light petroleum then afforded *methyl norlimonilyl ketone* (782 mg.), m. p. 110—112° (decomp., $[\alpha]_D$ +85° (*c* 1·10 in acetone), $\nu_{max.}$ 1736 (δ-lactone), 1722 (cyclohexanone with α-ether group), and 1712 (Me ketone) cm.$^{-1}$ (Found: C, 73·25; H, 6·9%; sap. equiv., 600. $C_{27}H_{32}O_8,2C_6H_6$ requires C, 73·1; H, 6·9%; equiv., 640). The presence of 2 mols. of benzene of crystallisation was confirmed by quantitative ultraviolet absorption and by the presence of the appropriate infrared bands. Precipitation of the compound from acetone with light petroleum gave benzene-free amorphous material, m. p. *ca.* 145°, showing no benzene absorption but only end-absorption, λ 207 mμ (ε 7000). Methyl norlimonilyl ketone did not crystallise except as the benzene solvate.

Methyl norlimonilyl ketone (71 mg.) was heated on the steam-bath with aqueous N-sodium hydroxide (6 ml.) for 1 hr. Working up gave back starting material (64 mg.), identified as the benzene solvate by m. p., mixed m. p., and rotation.

Methyl norlimonilyl ketone (41 mg.) in aqueous N-sodium hydroxide (10 ml.) was treated with excess of iodine in potassium iodide solution and left at room temperature. Iodoform was precipitated immediately and identified by m. p. and mixed m. p.

Derivatives of Methyl Norlimonilyl Ketone.—The ketone (2·31 g.) in ethanedithiol (50 drops) and tetrahydrofuran (5 ml.) was left at room temperature with toluene-*p*-sulphonic acid (3 g.) for 50 min. The solution was diluted with chloroform, extracted with aqueous N-sodium hydroxide, and evaporated. The crude product was filtered in benzene (25 ml.) through alumina (grade V; 10 g.), elution being with more benzene (50 ml.). Crystallisation from benzene–light petroleum afforded *methyl norlimonilyl ketone ethylene dithioketal* [LVI; X = $(\cdot S\cdot CH_2\cdot)_2$] (1·53 g.), m. p. 264—272°, $[\alpha]_D$ +57° (*c* 1·00 in acetone), $\nu_{max.}$ 1742 (δ-lactone) and 1729 (exalted cyclohexanone) cm.$^{-1}$ (Found: C, 62·15; H, 6·75; S, 11·65. $C_{29}H_{36}O_7S_2$ requires C, 62·1; H, 6·75; S, 11·65%). Limonin, treated under the same conditions, was recovered unchanged (520 mg. from 557 mg.).

In a preliminary experiment 3β-acetoxyallopregnane-11,20-dione (kindly provided by Messrs. Glaxo Laboratories Ltd.) (465 mg.) was left with ethanedithiol (10 drops) and boron trifluoride–ether complex (15 drops) at room temperature for 5 min. (crystalline deposit). Addition of methanol and working up in the usual way furnished 3β-*acetoxyallopregnane*-11,20-*dione* 20-(*ethylene dithioketal*) (554 mg.). Recrystallised from methylene dichloride–ethanol this (300 mg.) had m. p. 234—237°, $[\alpha]_D$ +22° (*c* 1·50), $\nu_{max.}$ 1725 (OAc) and 1695 (11-ketone) cm.$^{-1}$ (Found: C, 66·05; H, 8·5; S, 14·1. $C_{25}H_{38}O_3S_2$ requires C, 66·65; H, 8·5; S, 14·2%). This dithioketal (237 mg.) in ethanol (50 ml.) was refluxed with Raney nickel (activity W1, 2 g.) for 16 hr. Crystallisation of the product from aqueous methanol gave 3β-*acetoxyallopregnan*-11-*one*, m. p. 159—162°, $[\alpha]_D$ +38° (*c* 1·30), +40° (*c* 1·90) (Found: C, 76·6; H, 10·3; Ac, 11·85. $C_{23}H_{36}O_3$ requires C, 76·6; H, 10·05; Ac, 11·95%). In contrast, treatment of the dithioketal (125 mg.) in methanol (20 ml.), tetrahydrofuran (15 ml.), and water (2 ml.) with 3% lithium amalgam (5 g.) at room temperature with agitation for 20 hr. caused only hydrolysis of the acetate residue to furnish, after crystallisation from aqueous methanol, 3β-*hydroxyallopregnane*-11,20-*dione* 20-(*ethylene dithioketal*) (50 mg.), m. p. 242—246°, $[\alpha]_D$ +36° (*c* 0·60), $\nu_{max.}$ 3200 (OH) and 1697 (11-ketone) cm.$^{-1}$ (Found: C, 66·95; H, 8·65; S, 16·3. $C_{23}H_{36}O_3S_2$ requires C, 67·6; H, 8·85; S, 15·6%).

Relatively large quantities of lithium amalgam were prepared by the following safe procedure. Mercury (1 kg.) and lithium (33 g.) were heated at 350° for 12 hr. in a stainless-steel autoclave (500 ml. capacity). After cooling, the hard frothy amalgam was chipped out with a chisel and stored under light petroleum.

The dithioketal of methyl norlimonilyl ketone (1·04 g.) in ethanol (40 ml.), diluted with

aqueous 0·4N-sodium hydroxide (25 ml.) and water (10 ml.), was left at room temperature with agitation in the presence of 3% lithium amalgam (65 g.) for 20 hr. Working up gave the diol (880 mg.). Without purification this was taken up in pyridine (10 ml.), added to a suspension of chromium trioxide (2 g.) in pyridine (20 ml.), and left at room temperature for 20 hr., then poured into water. Destruction of the excess of oxidant with sulphur dioxide (cooling) and working up in the usual way gave neutral material (495 mg.) that was chromatographed over alumina (grade V, acid-washed; 8 g.) in benzene. Crystallisation from benzene–light petroleum then afforded the required *aldehyde* (LVII) (170 mg.), double m. p. 135°, 196—206°, $[\alpha]_D$ −132° (*c* 1·20 in benzene), $\lambda_{max.}$ 207—209 mμ (ε 8000), $\nu_{max.}$ 1749 (δ-lactone) and 1713 (CHO and 7-ketone) cm.$^{-1}$ (Found: C, 61·95; H, 6·7; S, 10·95. $C_{35}H_{36}O_7S_2$ requires C, 62·1; H, 6·45; S, 11·45%). The aldehyde group showed the characteristic τ value of −0·27 in its nuclear magnetic resonance spectrum.

Isolation of Obacunoic Acid.—Crushed grapefruit seeds (3 kg.) were extracted for limonin in the usual way. The mother-liquors remaining were taken to dryness (13·8 g.), dissolved in the minimum of acetone (about 20 ml.), and heated with an excess (about 150 ml.) of N-aqueous sodium hydroxide on the steam-bath for 1 hr., the acetone being allowed to evaporate. The reaction mixture was cooled, acidified with N-hydrochloric acid, and extracted with chloroform. The chloroform extract was shaken with excess of saturated sodium hydrogen carbonate solution and then discarded. The sodium hydrogen carbonate extract was acidified with N-hydrochloric acid and extracted with chloroform. The latter furnished an acid fraction (4·48 g.) which, on crystallisation from aqueous acetone or acetone–ether, gave obacunoic acid (1·4 g.), m. p. 205—208°, $[\alpha]_D$ −99° (*c* 1·06 in acetone), −103° (*c* 1·20 in tetrahydrofuran), $\lambda_{max.}$ 204—205 mμ (ε 18,000), λ_{210} mμ (ε 14,000), $\nu_{max.}$ 3220 (OH), diffuse absorption at 2800—3400 (CO_2H), 1745 (δ-lactone), 1710 (cyclohexanone and αβ-unsaturated CO_2H), and 1621 (C=C) cm.$^{-1}$ as well as the usual furan absorption (Found: C, 65·8; H, 6·85; active H, 0·4. Calc. for $C_{26}H_{32}O_8$: C, 66·1; H, 6·85; 2 active H, 0·45%).

Treatment of obacunoic acid (460 mg.) in tetrahydrofuran (25 ml.) with excess of ethereal diazomethane for 1 min. at room temperature (destruction of excess of diazomethane with one drop of formic acid) gave methyl obacunoate. Recrystallised from ether this (400 mg.) had m. p. 173—176°, $[\alpha]_D$ −94° (*c* 1·20 in CH_2Cl_2), −97° (*c* 0·73 in acetone), $\lambda_{max.}$ 205—206 mμ (ε 8400), $\nu_{max.}$ 3540 (OH), 1738 (δ-lactone), 1716 (αβ-unsaturated ester and cyclohexanone), and 1623 (C=C) cm.$^{-1}$ as well as the usual furan bands. Methyl obacunoate was also prepared by using 0·1N-sodium hydroxide and methyl iodide in acetone.

Obacunoic acid of analytical purity (5 mg.) in aqueous 2N-sodium hydroxide (3 ml.) was treated with an excess of aqueous iodine–potassium iodide solution. Iodoform (7 mg.) was precipitated; it was identified by sublimation and m. p. and mixed m. p. of the sublimate. The main acidic product (46 mg.) did not crystallise.

Hydrogenation of Obacunoic Acid and of its Methyl Ester.—Obacunoic acid (105 mg.) was hydrogenated over prereduced 10% palladised charcoal (150 mg.) in glacial acetic acid (10 ml.) (3·74 mols. uptake). The acidic product did not crystallise.

Methyl obacunoate (328 mg.) in acetic acid (25 ml.) was hydrogenated over prereduced 10% palladised charcoal (690 mg.) suspended in acetic acid (10 ml.) (3·86 mols. uptake). Crystallisation of the acidic product (220 mg.) from aqueous methanol furnished methyl hydrogen octahydro-obacunoninate (150 mg.), m. p. 173—175°, $[\alpha]_D$ +120° (*c* 1·10 in MeOH), $\nu_{max.}$ 3470 (OH), 3230 (CO_2H) 1741 and 1720 (saturated ester and CO_2H) and 1705 (cyclohexanone) cm.$^{-1}$. This methyl ester acid (83 mg.) was heated on the steam-bath with dioxan (2 ml.) and concentrated hydrochloric acid (2 ml.) for 16 hr. Working up in the usual way gave acidic (49 mg.) and neutral (30 mg.) fractions, neither of which crystallised. The acidic fraction showed $\lambda_{max.}$ 250 mμ (ε 9200) and had infrared bands at 1785 (γ-lactone), 1720 (CO_2H) and 1630 (hydrogen-bonded αβ-unsaturated cyclohexanone) cm.$^{-1}$. The neutral fraction had almost identical constants. Similar results were obtained with hydrogenated obacunoic acid (see above) as starting material.

Deoxyobacunoic Acid.—Obacunoic acid (136 mg.) in acetone (16 ml.) and acetic acid (6 ml.) was treated with aqueous N-chromous chloride (5 ml.) under nitrogen for 43 hr. at room temperature with constant agitation. The acetone was removed *in vacuo* and water (100 ml.) was added. Working up as usual gave, after crystallisation from methylene dichloride–benzene, *deoxyobacunoic acid* (107 mg.), m. p. 158—179°, $[\alpha]_D$ −98° (*c* 1·00 in CH_2Cl_2), $\lambda_{max.}$ 206—208 mμ (ε 22,600), λ_{210} mμ (ε 21,800), $\nu_{max.}$ 3360 (OH), 1715 and 1695 (αβ-unsaturated δ-lactone, CO_2H,

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and cyclohexanone) cm.$^{-1}$ as well as the usual furan bands (Found: C, 68·35; H, 7·15. $C_{26}H_{32}O_7$ requires C, 68·4; H, 7·05%).

Deoxyobacunoic acid (3·8 mg.) in methanol (2 ml.) and aqueous 2N-sodium hydroxide (2 ml.) was heated on the steam-bath for 90 min. Working up in the usual way gave acidic material which did not crystallise. It showed λ 206 (ε 10,000), 210 mμ (ε 7700).

Iso-obacunoic Acid.—Methyl obacunoate (122 mg.) in dry methanol (8 ml.) was added under nitrogen to a solution from sodium (500 mg.) in dry methanol (5 ml.) and refluxed for 1 hr. Water (10 ml.) was then added and the refluxing continued for 30 min. Acidification with N-hydrochloric acid and working up in the usual way (prolonged shaking with saturated sodium hydrogen carbonate was necessary to effect extraction) gave *iso-obacunoic acid* (XLIII). Recrystallised from methylene dichloride–benzene this (70 mg.) had m. p. 155—161°, $[\alpha]_D$ −41° (*c* 1·20 in CH_2Cl_2), $\lambda_{max.}$ 208 mμ (ε 5200), $\nu_{max.}$ 3000—3500 (diffuse CO_2H absorption), 1741 (δ-lactone), 1716 (CO_2H) and 1704 (cyclohexanone) cm.$^{-1}$ as well as the usual furan bands (Found: C, 65·95; H, 6·95. $C_{26}H_{32}O_8$ requires C, 66·1; H, 6·85%). Treatment of obacunoic acid under the same conditions also afforded iso-obacunoic acid but in inferior yield.

Iso-obacunoic acid (19·5 mg.) in glacial acetic acid (10 ml.) was hydrogenated over pre-reduced 10% palladised charcoal (65 mg.) until saturated (2·94 mols. uptake). The acidic product did not crystallise.

Iso-obacunoic acid (44 mg.) was treated under the usual conditions for the iodoform test (see under obacunoic acid above). No iodoform was produced and iso-obacunoic acid was recovered (30 mg.; correct m. p. and mixed m. p., and infrared spectrum).

Autoxidation of Obacunoic Acid.—Obacunoic acid (106 mg.) in t-butyl-alcoholic N-potassium t-butoxide was shaken under oxygen for 2 hr. (uptake of just over 1 mol. of oxygen). The product was worked up as in the comparable experiments in the limonin series (see above) to give the derived *diosphenol* (LIII; R = H) (103 mg.). Recrystallised from acetone–ethanol this (35 mg.) had m. p. 280—283°, $[\alpha]_D$ −160° (*c* 1·31 in acetone), $\lambda_{max.}$ 277 mμ (ε 4600), shifting reversibly in alkaline solution to $\lambda_{max.}$ 335 mμ (ε 3100), $\nu_{max.}$ 3484 (OH), 1737 and 1750 (lactones), 1690 (diosphenol) cm.$^{-1}$ as well as the usual furan bands (Found: C, 66·25; H, 6·45. $C_{26}H_{28}O_8$ requires C, 66·65; H, 6·02%). This diosphenol was neutral to sodium hydrogen carbonate solution. After treatment with diazomethane it was recovered unchanged. The diosphenols in the limonin series (see above) are also resistant to diazomethane and neutral to sodium hydrogen carbonate solution.

This diosphenol (73 mg.), treated with pyridine–acetic anhydride overnight at room temperature, gave an *acetate* (LIII; R = Ac). Recrystallised from acetone–ethanol this (52 mg.) had m. p. 277—279°, $[\alpha]_D$ −124° (*c* 1·26 in acetone), $\lambda_{max.}$ 210 mμ (ε 7100), 244 mμ (ε 3200), $\nu_{max.}$ 1751 (enol acetate), 1718 and 1704 (lactones), and 1658 (conjugated cyclohexanone) cm.$^{-1}$ (Found: C, 66·2; H, 6·1; Ac, 8·95. $C_{28}H_{30}O_9$ requires C, 65·85; H, 5·9; Ac, 8·4%). The acetate was recovered unchanged after treatment with diazomethane.

When iso-obacunoic acid (118 mg.) was autoxidised in the same way (see above) (rapid uptake of 1 mol. of oxygen) the product did not crystallise. However, it showed a normal diosphenol absorption [$\lambda_{max.}$ 276 mμ (ε 7700) changing reversibly to $\lambda_{max.}$ 340 mμ (ε 4700) in alkaline solution] and gave an acetyl derivative, also non-crystalline, which had $\lambda_{max.}$ 242 mμ (ε 10,000). The diosphenol gave a normal test with saturated aqueous sodium hydrogen carbonate and could be methylated with diazomethane to a non-crystalline methyl ester without affecting the diosphenol chromophore.

Treatment of Carvone Hydrate with Hypoiodite.—Carvone hydrate [30] (XLVII; X = O) (4·95 g.) in dioxan (50 ml.) was treated with aqueous 4N-sodium hydroxide (100 ml.) and iodine (30 g.) in water (100 ml.) containing potassium iodide (40 g.). The precipitated iodoform (6%) was removed and identified after sublimation by m. p. and mixed m. p. The filtrate was acidified and worked up as usual. The neutral fraction was divided into material insoluble in dilute sodium hydroxide, and enolic material (1·68 g.) (a dark oil with a strong phenolic odour and giving a green ferric chloride test). The crude phenolic fraction in pyridine (20 ml.) was heated on the steam-bath with 3,5-dinitrobenzoyl chloride (2·0 g.) for 30 min. Chromatography of the product over alumina gave 4,6-di-iodo-*o*-tolyl 3,5-dinitrobenzoate (XLVIII; R = dinitrobenzoyl) (900 mg., 5·6%). Recrystallised from ethanol this had m. p. and mixed m. p. 206—213° and an infrared spectrum identical with that of the authentic specimen described below.

In a second experiment the phenolic fraction (1·69 g.), obtained from carvone hydrate

(5·48 g.) as described above, was refluxed in aqueous 2N-sodium hydroxide (30 ml.) under nitrogen with zinc dust (10 g.) and iron powder (2 g.) for 2 hr. Working up in the usual way gave a phenolic oil (770 mg.) (Beilstein test negative). A portion of this material (460 mg.) in benzene (20 ml.) and pyridine (2 ml.) was refluxed with 3,5-dinitrobenzoyl chloride (2·2 g.) for 20 min. Crystallisation of the neutral product from ethanol gave *o*-tolyl 3,5-dinitrobenzoate (207 mg.), identified by m. p., mixed m. p., and infrared spectrum.

o-Cresol (5 g.) in aqueous 20N-ammonia (80 ml.) was treated with iodine (20 g.) and potassium iodide (25 g.) in water (40 ml.) at room temperature.[37] The precipitated 4,6-di-iodo-*o*-cresol was purified by crystallisation from glacial acetic acid (4·5 g.), m. p. 65—69°, then converted into the 3,5-*dinitrobenzoate* (see above) in the usual way. Recrystallised from ethanol this had m. p. 206—213° (Found: C, 31·15; H, 1·55; N, 5·15; I, 45·6. $C_{14}H_8I_2N_2O_6$ requires C, 30·35; H, 1·45; N, 5·05; I, 45·8%).

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[37] Datta and Prosad, *J. Amer. Chem. Soc.*, 1917, **39**, 441.

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49. *Precise Measurements, with the Glass Electrode, of the Ionization Constants of Benzoic, Phenylacetic, and β-Phenylpropionic Acids at 25°.*

By Edward J. King and J. E. Prue.

The ionization constants of three aromatic acids have been obtained from measurements on cells containing silver–silver chloride electrodes and glass electrodes of low resistance. The change in electromotive force was determined at the moment of transfer of the glass electrode between a cell containing a buffer solution of acetic acid and one containing a buffer solution of the weak acid under study. This comparison eliminates the effect of asymmetry potential. The behaviour of the glass electrode is more reproducible and accurate in transfers between buffer solutions of similar pH values than it is between hydrochloric acid and a buffer solution of a weak acid. At 25° the thermodynamic pK values for benzoic, phenylacetic, and β-phenylpropionic (dihydrocinnamic) acid are, respectively, 4·2050 ± 0·0015, 4·3074 ± 0·0010, and 4·6644 ± 0·0005$_5$. The precision of these measurements is thus as good as that obtainable with a hydrogen electrode.

One of the most convenient and precise methods of determining ionization constants of weak acids makes use of cells, without liquid junction, containing hydrogen and silver chloride electrodes. Because aromatic and unsaturated acids are reduced at the hydrogen electrode, the method is usually restricted to saturated aliphatic acids. There are, moreover, many inorganic acids that, because of their oxidizing action, cannot be studied with a hydrogen electrode. Recently it has been shown [1] that glass electrodes of low resistance give results with strong acids that are as precise as those obtained with the hydrogen electrode. We have now tested the performance of these glass electrodes in weak acid

[1] Covington and Prue, *J.*, 1955, 3696.

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buffers and have obtained ionization constants of three aromatic acids with a precision of better than 0·1 mv in electromotive force or 0·002 in pK.

In the earlier work on strong acids the change in electromotive force (ΔE) was determined for transfer of the glass electrode between solutions of the acid of different concentration. Because of the drift in asymmetry potential with time, it was necessary by a simple extrapolation to determine ΔE at the instant of transfer. We first attempted to apply this procedure to transfers of the glass electrode between the cells

$$\overline{\text{Ag|AgCl|HCl(0·12m)}}\,|\,\text{glass|HCl(0·01m)|AgCl|Ag}$$

and

$$\overline{\text{Ag|AgCl|HCl(0·12m)}}\,|\,\text{glass|HX(m), NaX(m), NaCl(m)|AgCl|Ag}$$

where HX represents the weak acid under study. The enclosed part on the left of the cells represents the glass electrode filled with hydrochloric acid and containing an internal silver–silver chloride reference electrode. Because the activity of 0·01m-hydrochloric acid is well established,[2] these measurements would give the ionization constant of the weak acid. It was unfortunately impossible to obtain results of satisfactory precision with our glass electrodes, for they frequently did not give the theoretical response when transfer was made between two solutions of widely different pH values, though it is possible that other carefully selected and protected glass electrodes may perform satisfactorily in such transfers.[3] In general one must expect considerable individuality in behaviour of glass electrodes, especially when a precision of better than 0·1 mv is required.

Satisfactory results were obtained by making transfers of the glass electrode between solutions that had similar pH values. We have used an acetate buffer as the reference solution in place of 0·01m-hydrochloric acid. Electromotive forces, E_s and E_x, were determined at the instant of transfer between cells S and X:

$$\text{Glass electrode|HOAc(0·01m), NaOAc(0·01m), NaCl(0·01m)|AgCl|Ag} \quad . \quad \text{(S)}$$

$$\text{Glass electrode|HX(m), NaX(m), NaCl(m)|AgCl|Ag} \quad . \quad . \quad . \quad . \quad \text{(X)}$$

It was assumed that the asymmetry potential of the glass electrode makes the same contribution to E_s and to E_x and is eliminated in taking the difference. Then we have:

$$\Delta E = E_s - E_x = -\frac{(\ln 10)\boldsymbol{R}T}{\boldsymbol{F}} \log \frac{m'_H\gamma'_H m'_{Cl}\gamma'_{Cl}}{m_H\gamma_H m_{Cl}\gamma_{Cl}} \quad . \quad . \quad . \quad . \quad (1)$$

where m′ and γ' are the molalities and activity coefficients in the standard buffer and m and γ are those in the buffer of cell X. If the hydrogen-ion activities are now eliminated by using the ionization constants of the acids, we obtain:

$$\frac{\boldsymbol{F}\Delta E}{(\ln 10)\boldsymbol{R}T} = pK_{HOAc} - pK_{HX} - \log \frac{m'_{Cl}}{m_{Cl}} - \log \frac{r'}{r} - \log \frac{\gamma'_{Cl}\gamma'_{HOAc}\gamma_X}{\gamma_{Cl}\gamma'_{OAc}\gamma_{HX}} \quad . \quad (2)$$

The buffer ratios are:

$$r' = m'_{HOAc}/m'_{OAc} = (0·01 - m'_H)/(0·01 + m'_H) \quad . \quad . \quad . \quad . \quad (3)$$

and

$$r = m_{HX}/m_X = (m - m_H)/(m' + m_H) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The hydrogen-ion molalities are small and are given with sufficient precision by $m'_H = K_{HOAc}$ and $m_H = K_{HX}$. We assume that the last term on the right of equation 2 is a linear function of the ionic strengths I' and I, and we can then write:

$$\log \frac{\gamma'_{Cl}\gamma'_{HOAc}\gamma_X}{\gamma_{Cl}\gamma'_{OAc}\gamma_{HX}} = B'I' - BI \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where B and B' are specific reaction constants.

[2] Bates, Guggenheim, Harned, Ives, Janz, Monk, Robinson, Stokes, Wynne-Jones, and Prue, *J. Chem. Phys.*, **1956**, **25**, 361.

[3] Covington, personal communication.

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Vol. 1961, page 276, line 1 *. *For* reaction *read* interaction.

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For acetic acid we take $pK = 4{\cdot}7567$ and $B' = -0{\cdot}061$.[4] We[5] have used $(\ln 10)\boldsymbol{RT}/\boldsymbol{F} = 59{\cdot}159$ mv. The equation for the calculation of the ionization constant of the acid HX relative to that of acetic acid at 25° then becomes:

$$pK_{HX} = 6{\cdot}759_4 - 0{\cdot}016904(\Delta E) + \log [m(m - m_H)/(m + m_H)] + BI \quad . \quad (6)$$

where ΔE is in mv. Because B was unknown, measurements were made on buffer solutions of six or seven different ionic strengths in cell X. The extrapolation function

$$Y = pK_{HX} - BI \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

was calculated directly from the experimental data, and pK_{HX} was found as the intercept at zero ionic strength.

Experimental

Materials.—Constant-boiling hydrochloric acid was chlorinated and boiled to eliminate bromide and iodide. A constant-boiling fraction, prepared by re-distillation, was diluted with conductivity water to give solutions of suitable strength. Sodium hydroxide was freed from carbonate by filtering a 50% solution of the " AnalaR " pellets. A stock solution was made by diluting the filtrate with conductivity water and was stored in a Polythene bottle equipped with a Pyrex siphon and protected with a soda-lime tube. No turbidity was obtained when this stock solution was mixed with 0·5N-barium chloride. The sodium hydroxide solution was initially standardized by weight-titration against standard hydrochloric acid and potassium hydrogen phthalate (National Bureau of Standards Sample 84f). The standardization against phthalate was rechecked three times. Sodium chloride of A.C.S. Reagent grade was purified and fused according to the directions of Pinching and Bates.[6] It contained less than 0·001% of bromide and 0·002% of sodium hydroxide. Silver oxide was precipitated by mixing very dilute solutions of silver nitrate and sodium hydroxide and was washed by decantation with water for a week. Conductivity water was prepared by passing distilled water through a column of mixed ion-exchange resins.

The benzoic acid was National Bureau of Standards Sample 39g., 99·99% pure. The phenylacetic and β-phenylpropionic (dihydrocinnamic) acid were products of the H.M. Chemical Company, Santa Monica, California. Both contained less than 0·004% of chloride, iron, phosphate, and heavy metals. Their purity was assayed by titration with standard sodium hydroxide solution. The phenylacetic acid was 99·98% pure; the other acid was 99·89% pure. " AnalaR " glacial acetic acid was fractionally frozen three times, one-third being discarded each time. A dilute solution was prepared and standardized against the sodium hydroxide solution.

Buffer solutions were prepared from weighed quantities of acid, sodium hydroxide, sodium chloride, and conductivity water. Buoyancy corrections were applied. It was convenient to prepare the standard acetate buffer of cell S by dilution of a more concentrated stock buffer. At least two different stock buffers were used in the determination of each ionization constant.

Electrodes.—These were similar to those used in previous work.[1] The glass electrodes were left for several weeks in 0·1M-hydrochloric acid and then were kept in either acetate or benzoate buffer. The electrodes were usually filled with 0·12m-hydrochloric acid; a few were used that contained the standard acetate buffer.

Apparatus.—The shielded leads were Telcon Type PT.1.GM.(Mod) non-microphonic cable (Telegraph Construction and Maintenance Co. Ltd., Mercury House, Theobalds Road, London, W.C.1.). The apparatus was otherwise virtually the same as that used previously. The temperature of the water thermostat was maintained at 25·00° ± 0·02°.

Experimental Procedure.—This too was similar to that in previous work. A glass electrode was brought to temperature equilibrium in a jar of acetate buffer in the thermostat. Then it was transferred successively to cell S, cell X, cell S, and cell X, being kept for 10 min. in each cell. Electrodes that gave useful results fell into two classes. The best electrodes usually showed a drift in potential of less than 0·05 mv during 10 min. in a given buffer. Their

[4] Harned and Ehlers, *J. Amer. Chem. Soc.*, 1932, **54**, 1350; Guggenheim and Prue, " Physico-chemical Calculations," 2nd edn., North-Holland Publ. Co., Amsterdam, 1956, pp. 338—339.

[5] Cf. Birge, *Reports Progr. Phys.*, 1941, **8**, 90.

[6] Pinching and Bates, *J. Res. Nat. Bur. Stand.*, 1946, **37**, 311.

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potential during the second immersion in a given buffer was within a few hundredths of a millivolt of its value during the first immersion. But the potential did show a gradual drift of several tenths of a millivolt from day to day. For these electrodes of the first class, ΔE was determined as in previous work by extrapolation to the moment of transfer.

Other electrodes showed a less steady response to transfers. The potential of one was steady for several minutes after transfer, then decreased. Others behaved in the opposite way; their potentials increased rapidly at first, then drifted gradually upwards. These changes were too great to permit concordant values of ΔE to be obtained by the extrapolation procedure. They were, however, sufficiently uniform from one buffer to the next to give steady values of ΔE at equal times after transfer in the two buffers. The average of these minute-by-minute values of ΔE agreed well with those obtained from the first class of electrode. When the minute-by-minute differences showed a marked trend or differed widely from one transfer to the next, the electrode was discarded. The instantaneous response to transfers of electrodes of the second class is apparently correct, and as long as deviations from this initia. value occur uniformly from one buffer to another, such electrodes give accurate results.

Results and Discussion

The molalities m for cell X and the changes in electromotive force with transfer ΔE are given in Table 1. With three exceptions the ΔE values are the average of the results from four glass electrodes or twelve transfers in all. For two buffers, only two glass electrodes were used; and for one buffer, only three. The average deviations of these

Table 1

m (mole kg.$^{-1}$)	ΔE (mv)	Y	m (mole kg.$^{-1}$)	ΔE (mv)	Y
	Benzoic acid			Phenylacetic acid	
0·005000	14·25 ± 0·07	4·2067	0·009000	23·44 ± 0·01	4·3126
0·007426	24·30 ± 0·09	4·2121	0·01000	26·16 ± 0·03	4·3131
0·01000	32·07 ± 0·06	4·2120	0·01249	31·96 ± 0·03	4·3125
0·01236	37·55 ± 0·08	4·2125	0·01500	36·50 ± 0·03	4·3156
0·01500	42·40 ± 0·11	4·2150	0·01890	42·98 ± 0·03	4·3159
0·02000	49·66 ± 0·11	4·2183	0·02500	49·49 ± 0·02	4·3191
			0·03000	53·92 ± 0·02	4·3237
	β-Phenylpropionic acid				
0·005000	−12·64 ± 0·06	4·6677			
0·007500	−2·18 ± 0·02	4·6688			
0·01000	+5·17 ± 0·02	4·6696			
0·01200	9·85 ± 0·02	4·6705			
0·01500	15·46 ± 0·03	4·6728			
0·02000	22·67 ± 0·03	4·6761			

mean values are given in the Table. The extrapolation functions Y, calculated from the data by means of equations 6 and 7, are also presented in Table 1. One result for β-phenylpropionic acid was discarded because it deviated widely from the rest, doubtless owing to some error in preparation of the solutions.

The values of pK and B in equation 7 were determined by the method of least squares. They are given in Table 2 together with their standard deviations, an indication of the reliability of the extrapolations. This Table also includes value of pK determined by other workers. All values of pK are for concentrations in moles per kg. of water.

Benzoic acid has been thoroughly investigated by several different methods and was used as a test of our technique. Our result was in good agreement with those of other workers. For β-phenylpropionic acid our result and the value from conductance measurements agree within the experimental errors. The agreement for phenylacetic acid is less good.

The B coefficients listed in Table 2 are all considerably larger than that of acetic acid (0·061 kg. mole^{-1}).

TABLE 2.

Acid	pK (This paper)	$-B$ (kg. mole^{-1})	pK (ref. *)
Benzoic	4·2050 ± 0·0015	0·335 ± 0·057	4·201 (*a*), 4·202 (*b*), 4·201 (*c*), 4·204 (*d*), 4·209 (*e*)
Phenylacetic	4·3074 ± 0·0010	0·253 ± 0·027	4·313 (*f*), 4·312 (*g*)
β-Phenylpropionic	4·6644 ± 0·0005$_8$	0·282 ± 0·022	4·661 (*h*)

* In parentheses.

Refs.: (*a*) Brockman and Kilpatrick, *J. Amer. Chem. Soc.*, 1934, **56**, 1483. (*b*) Saxton and Meier, *ibid.*, p. 1918. (*c*) Jones and Parton, *Trans. Faraday Soc.*, 1952, **48**, 8. (*d*) Robinson and Biggs, *Australian J. Chem.*, 1957, **10**, 128. (*e*) Kilpatrick and Arenberg, *J. Amer. Chem. Soc.*, 1953, **75**, 3812. (*f*) Dippy and Williams, *J.*, 1934, 161. (*g*) Jeffery and Vogel, *ibid.*, p. 166. (*h*) Dippy and Lewis, *J.*, 1937, 1008.

The coefficients can be separated into several contributions: [7]

$$B = B_{HX} + B_{Na,Cl} - B_{Na,X}$$

While the contributions $B_{Na,X}$ will doubless be considerably different for acetic acid and the aromatic acids, it is probable that the largest source of difference resides in B_{HX}, the contribution of the un-ionized acid. Self-interaction and, to a smaller extent, salt effects, are known to have large effects on the activity coefficients of benzoic and phenylacetic acid,[8] and the self-interaction effect is larger for benzoic than for phenylacetic acid. Qualitatively the B parameters in Table 2 increase as the solubility of the acid in water decreases.

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READING UNIVERSITY. [*Received, July 15th*, 1960.]

[7] Guggenheim and Turgeon, *Trans. Faraday Soc.*, 1955, **51**, 747.
[8] Long and McDevit, *Chem. Rev.*, 1952, **51**, 119; Paul, *J. Amer. Chem. Soc.*, 1953, **75**, 2513.

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50. *The Structure of Evolidine.*

By H. D. LAW, I. T. MILLAR, and H. D. SPRINGALL.

The cyclic heptapeptide nature of evolidine has been confirmed. The sequence of the amino-acid residues has been investigated and evidence obtained for the mode of linkage of the aspartyl residue. The structure proposed for evolidine is

cyclo[Ser.Phe.Leu.Pro.Val.Asp-(β-NH_3).Leu].*

The amino-acids obtained on hydrolysis are shown all to have the L-configuration.

EVOLIDINE was isolated from the leaves of *Evodia xanthoxyloides* and characterised by Hughes, Neill, and Ritchie.[2] It is insoluble in water or dilute aqueous alkali or acid, but readily soluble in acetone or ethanol. It crystallises from ethanol in colourless prisms, m. p. 277—279°, $[\alpha]_D^{16}$ −129° (*c* 0·45 in EtOH). *X*-Ray studies by Curtis [3] gave an estimate of 769 ± 6 for the molecular weight.

The substance did not form an *N*-acetyl derivative, even on vigorous treatment with acetic anhydride, but on hydrolysis gave in high yield a mixture of α-amino-acids and ammonia. Preliminary analysis of this mixture and a consideration of the properties of

* The abbreviations used for the amino-acids are those suggested by Brand and Edsall.[1]

[1] Brand and Edsall, *Ann. Rev. Biochem.*, 1947, **16**, 223.
[2] Hughes, Neill, and Ritchie, *Austral. J. Agric. Res.*, 1952, *A***5**, 401.
[3] Eastwood, Hughes, and Ritchie, with *X*-ray studies by Curtis, *Austral. J. Chem.*, 1955, **8**, 552.

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evolidine led Hughes and his co-workers to suggest that the substance is probably a cyclic heptapeptide of composition Val, Leu_2, Pro, Phe, Ser, Asp-NH_2 (required: *M*, 771).

A specimen of evolidine was given to us by Professor A. J. Birch, F.R.S. We have investigated the structure of the substance with regard to (i) its cyclic nature, (ii) its amino-acid composition, (iii) the sequence of the amino-acid residues in the molecule and (iv) the configuration of the amino-acid residues; and a brief account of the findings has been given.[4]

(i) *Cyclic Nature.*—Evolidine does not yield a 2,4-dinitrophenyl derivative when treated with 1-fluoro-2,4-dinitrobenzene in suspension in aqueous sodium hydrogen carbonate at room temperature or when methanol has been added to dissolve the evolidine. This observation and the neutral character of the substance indicate a cyclic peptide structure.

(ii) *Amino-acid Composition.*—The amino-acids in the hydrolysate of evolidine were separated by the ion-exchange method due to Moore and Stein [5] and estimated colorimetrically after reaction with ninhydrin.[6] The composition found (Table 1) agrees with that postulated by Hughes and his co-workers.[2,3]

TABLE 1.

Amino-acid	Amino-acid (g. per 100 g. of peptide)	Residue ·HN·CHR·CO· (g.) per 100 g. of peptide	No. of residues calc. for *M* 771
Aspartic acid *	16·89	14·60	0·98 ≡ 1
Serine	14·25	11·80	1·05 ≡ 1
Proline	14·71	13·16	1·05 ≡ 1
Valine	15·44	13·06	1·02 ≡ 1
Leucine	33·36	28·77	1·96 ≡ 2
Phenylalanine	21·78	19·41	1·02 ≡ 1
Total	116·43	100·80	7·08 ≡ 7

* The aspartic acid is present in the peptide as asparagine.

(iii) *Sequence of Amino-acid Residues.* Specimens of evolidine were partially hydrolysed by concentrated hydrochloric acid at 35° for times ranging from 15 to 72 hours. Similar partial hydrolyses were carried out at 80°, for up to 6 hours. The amino-acids and oligopeptides produced were separated by two-dimensional paper chromatography and by electrophoresis.

The two-dimensional chromatograms (butan-1-ol–acetic acid–water, and phenol–water) varied somewhat. A general and composite diagram of the ninhydrin pattern is illustrated.

The chromatogram of the products of hydrolysis at 35° for 44 hours consisted of the characteristic spots of the six constituent amino-acids and the ninhydrin positive areas A and B_2: with longer hydrolyses, an area B_1 appeared; after hydrolyses for 72 hours, the aspartic acid spot was intensified, area A was missing, and areas B_1 and B_2 were fainter. Hydrolysis in the 15—44 hour range gave an unresolved mixture of ninhydrin-positive material in the valine–phenylalanine–leucine area and also a separate area C.

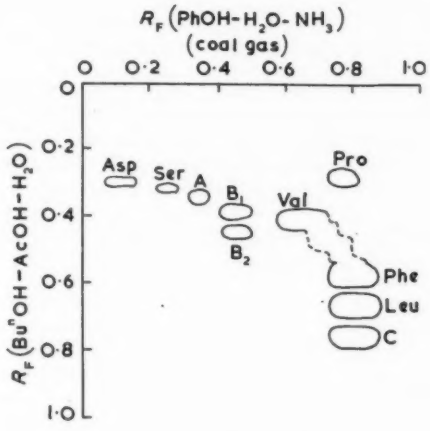
The areas A, B_1, B_2, and C were located on fresh chromatograms by ultraviolet light and were then eluted, and studied individually by a combination of the following techniques: (*a*) identification of the amino-acid components (hydrolysis followed by paper chromatography); (*b*) *N*-terminal-residue sequence studies by Sanger's fluorodinitrobenzene method [7] or Edman's stepwise phenyl isothiocyanate method; [8] (*c*) *C*-terminal-residue sequence studies by the carboxypeptidase method.[9]

[4] Law, Millar, Springall, and Birch, *Proc. Chem. Soc.*, 1958, 198.
[5] Moore and Stein, *J. Biol. Chem.*, 1951, **192**, 663.
[6] Moore and Stein, *J. Biol. Chem.*, 1948, **176**, 367.
[7] Sanger, *Biochem. J.*, 1945, **39**, 507; Sanger and Thompson, *ibid.*, 1953, **53**, 353, 366; Levy, *Methods Biochem. Analysis*, 1955, **2**, 360.
[8] Edman, *Acta Chem. Scand.*, 1950, **4**, 283; 1953, **7**, 700; Fraenkel-Conrat, *Methods Biochem. Analysis*, 1955, **2**, 383.
[9] Harris, *Methods Biochem. Analysis*, 1955, **2**, 397.

Area A (from hydrolysis at 80° for 6 hours) consists of valine and aspartic acid in equimolecular proportions (estimated by the dinitrophenyl technique [10]), all the valine being *N*-terminal; the A-peptide is therefore valylaspartic acid.

Areas B_1 and B_2 (from hydrolysis at 80° for 6 hours) each consist of aspartyl-leucine dipeptides.

Electrophoresis on paper at pH 6·7 of materials B_1 and B_2 showed identical rates of anionic migration; in the pH range 6—3, the rates of anionic migration were in the order, aspartic acid > B_2 > B_1; at pH <3 the rates of cationic migration were in the order,



B_2 > aspartic acid > B_1. These findings show that neither B_1 nor B_2 is an asparaginyl-peptide and are compatible with the identification B_1 = β-Asp.Leu, B_2 = α-Asp.Leu. Material B_1 gives the blue (rather than purple) ninhydrin colour characteristic of β-aspartyl-peptides.

Authentic α-aspartyl-leucine, given to us by Dr. G. T. Young, proved to be chromatographically identical with B_2. A sample of material B_2 was heated at 100° for some hours (under these conditions α-aspartylvaline, α-aspartyltyrosine, and α-aspartylglutamic acid rearrange partially to the β-aspartyl isomers [11]) and was then chromatographed. Two ninhydrin-positive areas appeared, identical with B_1 and B_2 in colour and location. Since (*a*) the same effect was observed when the α-aspartyl-leucine was heated in acid solution under the conditions used for the partial hydrolyses, (*b*) on chromatograms of mixtures obtained by brief hydrolysis of evolidine, area B_2 appeared strongly, while B_1 was only faint or absent, and (*c*) β-aspartylvaline does not rearrange to the α-isomer,[11] it is felt (i) that the identification of materials B_1 and B_2 as β- and α-aspartyl-leucine respectively is established and (ii) that the α-isomer is the original species in evolidine, the β-isomer arising from it during hydrolysis.

Area C was investigated as follows. An evolidine hydrolysate (80° for 1 hour) was subjected to electrophoresis, which separated the hydrolysate mixture into three zones. These were eluted and found to consist respectively of (*a*) aspartic acid, (*b*) materials A, B_1, and B_2, (*c*) the remaining components. Paper chromatography (butanol–acetic acid–water) of the eluate from the last zone separated material C into three regions, C_1, C_2, and C_3, the last having an R_F value very close to that of valine. Material from C_1, when

[10] Levy, *Nature*, 1954, **174**, 126; Levy and Chung, *J. Amer. Chem. Soc.*, 1955, **77**, 2899; Levy, *Methods Biochem. Analysis*, 1955, **2**, 360.

[11] Le Quesne and Young, *J.*, 1952, 24; John and Young, *J.*, 1954, 2870.

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treated with fluorodinitrobenzene and then hydrolysed, gave a high yield of *N*-dinitrophenylleucine, while that from C_3 gave *N*-dinitrophenylphenylalanine. (Both regions gave traces of dinitrophenylserine presumably owing to contamination with traces of serine or seryl peptides.) The free acids found in this process from both materials C_1 and C_2 were valine, leucine, proline, and aspartic acid. Application of the Edman technique to materials C_1 and C_2 indicated that the *N*-terminal sequences are Leu.Pro.Val . . . and Phe.Leu.Pro . . . respectively. The action of carboxypeptidase [9] on the mixture C_1–C_2 liberated leucine exclusively.

The findings on these peptides are therefore:

$$C_1 = \text{Leu.Pro.Val.(Asp)Leu}$$
$$C_2 = \text{Phe.Leu.Pro.(Val.Asp)Leu}$$

A hydrolysate of the material eluted from area C_3 contained serine, valine, and phenylalanine and only minute traces of other amino-acids. The fluorodinitrobenzene technique for *N*-terminal-residue identification gave dinitrophenyl-serine and -valine. The only free amino-acid present was phenylalanine. Since valine had been shown to occur in the sequence . . . Val.Asp . . ., material C_3 is probably a mixture of serylphenylalanine and free valine.

The structures of the five peptides described permit the sequence of the amino-acid residues in evolidine to be uniquely assigned:

Asp.Leu	B_1 and B_2
Val. Asp	A
Leu.Pro. Val.(Asp)Leu	C_1
Phe.Leu.Pro.(Val. Asp)Leu	C_2
Ser.Phe	C_3
Ser.Phe.Leu.Pro. Val. Asp.Leu	

(iv) *Configuration of Amino-acid Residues.*—A hydrolysate of evolidine was treated with fluorodinitrobenzene and the resulting mixture of products was separated by partition chromatography on columns of buffered " Hyflo Super Cel ". The following fractions were obtained (all dinitrophenylamino-acids): (*a*) serine and aspartic acid, (*b*) proline, (*c*) valine and some 2,4-dinitrophenol, (*d*) leucine and phenylalanine. Mixture (*d*) was resolved and the compositions of materials (*a*), (*b*), (*c*), and (*d*) were determined quantitatively by one-dimensional paper chromatography.

The directions of optical rotation of the dinitrophenyl derivatives in these fractions all agreed with those reported for the appropriate L-amino-acid derivatives.[12] Those $[M]_D$ values estimated were in agreement with the published values.[12]

The total evidence thus indicates that evolidine has the structure:

cyclo(-L-Ser-L-Phe-L-Leu-L-Pro-L-Val-L-Asp(β-NH_2)-L-Leu-)

Experimental

Hydrolysis of Evolidine.—(a) *Complete.* Specimens (~10 mg.) of evolidine (recrystallised six times from aqueous ethanol) were weighed into tubes of 6 mm. bore. Constant-boiling hydrochloric acid (1 ml.) was added, the mixtures were frozen, and the tubes evacuated, sealed, and heated at 105° for 20 hr. The contents of each tube were then diluted with water (2 ml.) and evaporated to dryness *in vacuo* over sodium hydroxide.

(b) *Partial.* The conditions were similar to those used for the complete hydrolyses, except that the solutions were heated in 5 ml. stoppered flasks at 35° ± 0·25° for 15—72 hr. or 80° ± 0·1° for 2—6 hr.

Amino-acid Analysis.—(a) *Identification.* The amino-acids in mixtures were identified by comparison with authentic specimens (Roche Products Ltd.) on single-dimension paper chromatograms on Whatman No. 1 paper. Various solvent systems were used, especially

[12] Rao and Sober, *J. Amer. Chem. Soc.*, 1954, **76**, 1328.

butan-1-ol–acetic acid–water (4 : 1 : 5) and " mixture P " (butan-1-ol–butan-2-one–water–dicyclohexylamine, 10 : 10 : 5 : 2). Ninhydrin (" AnalaR " grade; 0·025% in acetone) was used to detect the amino-acids, by spraying and heating at 105° for 10 min.

(b) *Estimation.* The amino-acids were estimated by the Moore–Stein procedure of ion-exchange adsorption separation, elution,[5] and eluate analysis by quantitative colorimetry of the ninhydrin reaction.[6]

The ion-exchange column (100 cm. long; bore 0·9 cm.) was packed with Dowex-50-X8 sulphonated polystyrene resin (supplied by Greeff and Co. Ltd.) and was thermostatically controlled to run within ±0·25° in the range 37·5° to 75°.

Each estimation was performed on a weighed specimen of ~5 mg. of the amino-acid mixture (dissolved in citrate buffer of pH 3·41). The elution was carried out by citrate buffer solutions, of pH 3·42 at 37·5° in the initial stages and of pH 4·25 at 75° in the later stages, and was complete after about 125 hr. The eluate (about 500 ml. in all) was collected in an automatic fraction-collector designed at the National Institute for Medical Research, Mill Hill,[13] and supplied by Towers and Co. Ltd. The amino-acid concentration in each fraction was estimated by measuring, in a Unicam S.P. 500 ultraviolet spectrophotometer, the optical density at 570 mμ of the colour produced by reaction with ninhydrin under Moore–Stein standardised conditions.[6]

Analysis of Products of Partial Hydrolysis of Evolidine.—Chromatograms of the partial hydrolysates were prepared on Whatman No. 1 paper, according to Sanger and Tuppy's directions.[14] After development in the first dimension with phenol, the solvent was removed by suspending the paper in a strong draught in a fume cupboard at room temperature for 2 days. The peptides and amino-acids for further investigation were located by fluorescence in ultra-violet light after the paper had been heated at 105° for 20 min.[15] On single-dimension chromatograms the material for separation was applied as a line at the origin. The positions of bands on the chromatograms were located by fluorescence and were confirmed by cutting vertical strips from the paper and treating them with ninhydrin. For two-dimensional chromatograms the second solvent was butanol–acetic acid–water.

Electrophoresis was carried out on Whatman No. 1 paper, supported between strips of plate glass and dipping at each end into the electrode dishes.[16] 0·05M-Ammonium acetate (pH ~6·7) was used as solvent. After 5 hr. with a potential difference of 500 v, aspartic acid moved 10—12 cm. towards the anode; materials B_1, B_2, and A moved 4—6 cm. towards the anode; and the other products of hydrolysis stayed near to the origin. Whatman No. 31 paper gave more even bands but these did not fluoresce well.

Material was removed from particular areas of the chromatogram and electrophoresis papers by the capillary method.[17] It was taken to dryness and stored for further investigation.

Identification of N-Terminal Residues.—The *N*-terminal residues of peptides were identified by the fluorodinitrobenzene technique, as described by Levy. The dinitrophenyl derivatives of the constituent amino-acids of evolidine, except for those of leucine and phenylalanine, are separated on paper in the toluene-type solvent described by Levy. *N*-Dinitrophenyl-leucine and -phenylalanine are readily separated in 1·5M-phosphate.

Stepwise Degradations.—The phenyl isothiocyanate method for determination of *N*-terminal-residue sequence was used, virtually as described by Fraenkel-Conrat,[8] the cyclisation of the phenylthiocarbamoyl-peptides to the corresponding phenylthiohydantoins being followed by observing the shift of the ultraviolet absorption maxima from 240 to 268 mμ.

The modifications used were: (i) During the formation of the phenylthiocarbamoyl-peptides, the pH was tested by B.D.H. narrow-range (8·5—10) indicator paper and kept in the range 8·7—9·0 by adding aqueous 0·01N-sodium hydroxide. The solutions were stirred by a stream of nitrogen. (ii) The aqueous solutions of the phenylthiocarbamoyl-peptides remaining after the extraction of excess of phenyl isothiocyanate were freed from dissolved benzene by a stream of nitrogen.

The phenylthiohydrantoins were identified by chromatography, and by chromatography of the amino-acids regenerated from them by acid hydrolysis. Traces of contaminating amino-acids (from non-specific cleavage of the peptides) were present at all stages.

[13] Lister, *Chem. and Ind.*, 1955, 583.
[14] Sanger and Tuppy, *Biochem. J.*, 1951, **49**, 463.
[15] Phillips, *Nature*, 1948, **161**, 53.
[16] Linstead, Elvidge, and Whalley, " Modern Techniques of Organic Chemistry," Butterworths Sci. Publ., London, 1955, p. 33.
[17] Consden, Gordon, and Martin, *Biochem. J.*, 1947, **41**, 590; Sanger and Tuppy, *ibid.*, 1951, **49**, 463.

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Identification of C-Terminal Residues.—This was carried out by Harris's enzymic method,[9] using carboxypeptidase (Light and Co. Ltd.) treated with di-isopropyl phosphofluoridate (provided by Dr. B. C. Saunders) to inhibit endopeptidase action.

Rearrangements of Aspartyl Peptides.—α-Aspartyl-leucine (1 mg.) was heated in solution in water (0·1 ml.) in a sealed tube at 100° for 6 hr. Chromatography of the resulting solution showed the presence of α-aspartyl-leucine (strong), β-aspartyl-leucine (strong), aspartic acid (trace), and leucine (trace).

α-Aspartyl-leucine (1 mg.) was heated in solution in concentrated hydrochloric acid (0·1 ml.) in a sealed tube at 35° for 2 days. Electrophoresis of the resulting solution in 10% acetic acid showed the presence of α-aspartyl-leucine (strong), β-aspartyl-leucine (faint), aspartic acid (strong), and leucine (strong). After hydrolysis for 7 days at 35°, appreciable amounts of β-aspartyl-leucine were present as well as the other components.

When a solution of α-aspartyl-leucine in concentrated hydrochloric acid was heated at 80°, β-aspartyl-leucine appeared on chromatograms after 4 hr.

Assignment of Configuration to the Amino-Acids from Evolidine.—The mixture of amino-acids obtained on complete hydrolysis of evolidine (80 mg.) was converted into mixed dinitrophenyl derivatives by Levy's method [10] (treatment in mildly alkaline aqueous solution with fluorodinitrobenzene, extraction of the excess of this with ether, acidification, extraction of the dinitrophenyl derivatives with ether).

The mixture was separated into its components by an adaptation and combination of the methods due to Perrone [18] and to Levy.[10]

Three columns were set up, in series, containing " Hyflo Super Cel " supporting aqueous phases made up of citric acid–phosphate buffers of pH 4, 6·5, and 7 severally. The mixture of dinitrophenylamino-acids in ether was placed at the top of the pH 4 column and the chromatogram developed and eluted with ether. The eluate of the fast-moving band was passed on to the pH 6·5 column: that from the slow-moving band was collected. The process was repeated with the columns of pH 6·5 and pH 7. The fractions thus obtained were the slow bands from (*a*) col. pH 4, (*b*) col. pH 6·5 (*c*) col. pH 7, and (*d*) the fast band from col. pH 7. (A very fast-moving band on col. pH 7 was due to 2,4-dinitroaniline and was discarded.) These fractions were further separated by paper chromatography on Whatman No. 3 paper [ether–aqueous phosphate buffer (NaH_2PO_4, M; $+Na_2HPO_4$, 0·5M). They were identified as dinitrophenyl derivatives of: (*a*) serine and aspartic acid; (*b*) proline; (*c*) valine (and 2,4-dinitrophenol); (*d*) leucine and phenylalanine.

The optical rotations of these systems, in solution in 4% aqueous sodium hydrogen carbonate, were examined in a Bellingham and Stanley micropolarimeter. The concentrations of the solutions of dinitrophenyl derivatives of (i) an equimolecular serine–aspartic acid mixture, (ii) valine, and (iii) leucine were estimated from measurements of the extinction coefficients at 360 mμ, and thence the corresponding $[M]_D^{25}$ values were calculated. The results are given in Table 2.

TABLE 2.

Dinitrophenyl derivatives of	Observed rotation Sense	$[M]_D^{25}$	Recorded [13] for L-enantiomorph
Serine + aspartic acid	+	319°	+308°
Proline	—		−2172°
Valine	+	290°	+309°
Leucine	+	155°	+168°
Phenylalanine	—		−261°

We are indebted to Professor A. J. Birch, F.R.S., for a supply of evolidine, to Dr. G. T. Young for a specimen of α-aspartyl-leucine, to Dr. B. C. Saunders for di-isopropyl phosphofluoridate, to Professor G. W. Kenner, Dr. I. J. Harris, Dr. T. S. Work, and Dr. S. Jacobs for helpful discussions, to the Royal Society and to Imperial Chemical Industries Limited for grants and to the D.S.I.R. for a Research Studentship (to H. D. L.).

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[18] Perrone, *Nature,* 1951, **167**, 513.

51. *Alkyls and Aryls of Transition Metals. Part IV.* Cobalt(II) and Iron(II) Derivatives.*

By J. Chatt and B. L. Shaw.

The preparation and properties of stable organometallic complexes of the types *trans*-$[MR_2(PR'_3)_2]$ (M = Co, Fe; R, R' = organic radicals) are described. The groups R are *ortho*-substituted aryl groups where the substituents are somewhat bulky. These are the first planar complexes of cobalt(II) and iron(II) having only monodentate ligands. Their configurations were established by their magnetic and electric dipole moments. Possible reasons for the unusual configurations and stabilities of these organometallic derivatives are discussed.

Very few stable alkyl or aryl derivatives of cobalt or iron are known although several unstable compounds have been described. With cobalt these include the very unstable $[CoMe(CO)_4]$ (ref. 1) and some ill-defined α- and β-naphthylcobalt derivatives.[2,3] Some acetylides of the types $K_4[Co(C{\equiv}CR)_6]$ and $K_3[Co(C{\equiv}CR)_6]$ have also been described.[4]

Stable iron derivatives of the type $[FeR(\pi\text{-}C_5H_5)(CO)_2]$ (R = alkyl or aryl) have been prepared,[5] and iron also gives unstable acetylides of the types $K_4[Fe(C{\equiv}CR)_6]$ and $K_3[Fe(C{\equiv}CR)_6]$.[4,6]

After the preparation of very stable alkyls, aryls, and ethynyls of platinum(II) of the types $[PtXRL_2]$ and $[PtR_2L_2]$ (R = alkyl, aryl, or substituted ethynyl; L = tertiary phosphine, arsine, or sulphide),[7,8] and of aryl- and ethynyl-nickel(II) complexes[9] $[NiXR(PR'_3)_2]$ and $[NiR_2(PR'_3)_2]$ (where R = *ortho*-substituted aryl or substituted ethynyl radical) we have now prepared similar compounds of cobalt(II) and a compound of iron(II). These complexes are only of the type *trans*-$[MR_2(PR'_3)_2]$ (M = Co, Fe; R = *ortho*-substituted aryl group) and are less stable than the corresponding nickel complexes. In a given series of aryl complexes $[MR_2(PR'_3)_2]$ the stabilities fall off markedly in the order of M, nickel > cobalt > iron. In general these organometallic complexes were prepared in a similar way to their nickel(II) analogues, by reaction of a Grignard reagent or lithium compound with a tertiary phosphine–metal halide complex. The products were hydrolysed (usually with dilute halogen acid); the desired complex was then precipitated or could be isolated from the organic layer:

$$[CoBr_2(PEt_2Ph)_2] + 2MgBrR \longrightarrow [CoR_2(PEt_2Ph)_2] + 2MgBr_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$[FeCl_2(PEt_2Ph)_2] + 2MgBrR \longrightarrow [FeR_2(PEt_2Ph)_2] + 2MgClBr + 2PEt_2Ph \quad . \quad . \quad . \quad . \quad (2)$$

Attempted Preparation of Alkylcobalt(II) and Cobalt Acetylide Derivatives.—Addition of $[CoBr_2(PEt_2Ph)_2]$ to ethereal methylmagnesium bromide at −65° gave an olive-green solution which on warming to −40° rapidly became dark brown. The product of this reaction was very unstable and no methylcobalt derivative could be isolated. Using methyl-lithium instead of the Grignard reagent gave similar results.

Treatment of bis(tertiary phosphine)cobaltous halides with (1) phenylethynylmagnesium bromide in ether or (2) lithium phenylacetylide in ether gave dark brown or reddish-brown amorphous products from which no cobalt–phenylacetylide complex could be

* Part III, *J.*, 1960, 1718.

1 Hieber, Vohler, and Braun, *Z. Naturforsch.*, 1958, **13b**, 192.
2 Ingles and Polya, *J.*, 1949, 2280.
3 Briggs and Polya, *J.*, 1951, 1615.
4 Nast, *Angew. Chem.*, 1960, **72**, 26.
5 Piper and Wilkinson, *J. Inorg. Nuclear Chem.*, 1956, **3**, 104.
6 Nast and Urban, *Z. anorg. Chem.*, 1956, **287**, 17.
7 Chatt and Shaw, *J.*, 1959, 705.
8 Chatt and Shaw, *J.*, 1959, 4020.
9 Chatt and Shaw, *J.*, 1960, 1718.

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isolated. Neither could one be isolated on use of sodium phenylacetylide in liquid ammonia.

Arylcobalt(II) *Derivatives.*—Addition of the turquoise-blue complex $[CoBr_2(PEt_2Ph)_2]$ to mesitylmagnesium bromide at −30° resulted in the rapid formation of an olive-green reaction mixture which slowly became reddish-brown. The intermediate olive-green substance was probably $[CoBr(mesityl)(PEt_2Ph)_2]$ but this compound appears to be very labile and soluble and attempts to isolate it were unsuccessful. From the final reddish-brown mixture the golden-yellow *trans*-$[Co(mesityl)_2(PEt_2Ph)_2]$ was readily isolated in *ca.* 80% yield. This compound was stable in cold benzene solution, especially in the absence of air, but it decomposed rapidly in hot benzene. A poorer yield was obtained by the action of mesityl-lithium on $[CoBr_2(PEt_2Ph)_2]$. Other aryl groups giving stable arylcobalt derivatives were 2-biphenylyl, 2-methyl-1-naphthyl, and pentachlorophenyl. The pentachlorophenyl complex was most stable: thus $[Co(C_6Cl_5)_2(PEt_2Ph)_2]$ did not decompose below 220° and was moderately stable in boiling benzene. The other arylcobalt complexes decomposed completely below 150° and also in hot benzene. The diarylcobalt complexes of the type $[Co(aryl)_2(PEt_2Ph)_2]$ have very small or zero dipole moments, indicating a *trans*-planar configuration.

The phenyl, *o*-tolyl, *o*-chlorophenyl, *o*-bromophenyl, α-naphthyl, and 9-anthryl groups all appeared to give similar cobalt complexes which, however, decomposed on attempted isolation. Diethylphenylphosphine, of the phosphines tried, gave the most readily crystallisable and stable arylcobalt derivatives; the corresponding triethylphosphine–arylcobalt complexes were less stable.

One would expect these planar diarylcobalt(II) complexes to have one unpaired electron. Magnetic-susceptibility measurements on the solid compounds at 20° indicated magnetic moments of 2·3—2·7 B.M. These values are consistent with a planar cobalt(II) complex with one unpaired electron, since such complexes appear to have a large orbital contribution to the magnetic moment. For example, Figgis and Nyholm [10] found the magnetic moments of some planar cobalt(II) complexes with chelate ligands to be as high as 2·9 B.M.

Attempts to prepare Monoarylcobalt(II) *Complexes.*—As mentioned above, the addition of $[CoBr_2(PEt_2Ph)_2]$ to solutions of arylmagnesium bromides first gave very unstable olive-green complexes, probably $[CoBr(aryl)(PEt_2Ph)_2]$, which could not be isolated. In the nickel series analogous monoarylnickel complexes were readily prepared from diarylnickel complexes by fission with dry hydrogen chloride (1 mol.), but attempts to obtain monoarylcobalt complexes in this way were not successful. On addition of dry hydrogen chloride (1 mol.) to a solution of *trans*-$[Co(mesityl)_2(PEt_2Ph)_2]$ the solution became olive-green but, on isolation, unchanged starting material (*ca.* 50% recovery) and a bluish-green, very labile product strongly smelling of diethylphenylphosphine, were obtained: the second product was probably impure $[CoCl_2(PEt_2Ph)_2]$.

Aryliron(II) *Complexes.*—Since bis(pentachlorophenyl)bis(diethylphenylphosphine)-cobalt(II) was so stable it seemed possible that an analogous iron(II) complex might be stable. The necessary starting materials, *e.g.*, $[FeX_2(PEt_2Ph)_2]$, are unknown although analogous triphenylphosphine complexes $[FeX_2(PPh_3)_2]$ have been described briefly.[11,12] When anhydrous ferrous chloride and diethylphenylphosphine (>4 mol.) were boiled together in benzene the ferrous chloride gradually dissolved to give a colourless solution, possibly containing the octahedral complex $[FeCl_2(PEt_2Ph)_4]$. Removal of the solvent gave the complex as very soluble colourless crystals which rapidly became green in air. Addition of the crude benzene solution of this ferrous chloride–diethylphenylphosphine complex to a solution of pentachlorophenylmagnesium chloride gave the golden-yellow complex $[Fe(C_6Cl_5)_2(PEt_2Ph)_2]$. This iron complex was much less stable than the analogous cobalt complex and was partially decomposed after being dissolved in benzene at 25° for

[10] Figgis and Nyholm, *J.*, 1954, 12; 1959, 338.
[11] Hieber and Floss, *Z. anorg. Chem.*, 1957, **291**, 314.
[12] Naldini, Internat. Conference Pure Appl. Chem., Munich, 1959.

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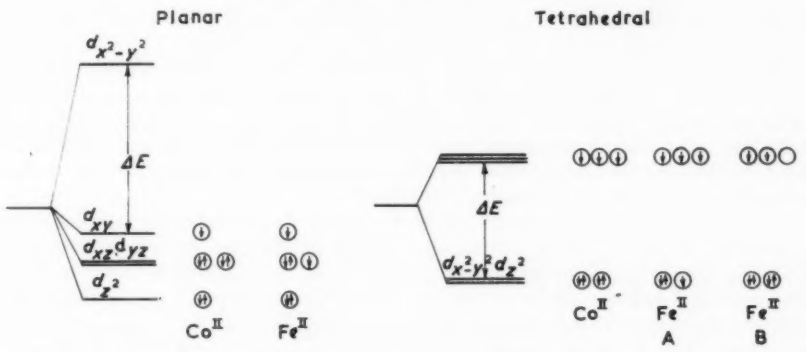
several minutes. This made a determination of the dipole moment difficult. The compound was shown by an *X*-ray powder diagram to be isomorphous with the corresponding cobalt complex and therefore of *trans*-planar configuration. The magnetic moment of 3·6 B.M. is consistent with the planar arrangement of ligands and two unpaired electrons.

Adding the crude ferrous chloride–diethylphenylphosphine complex to a solution of mesitylmagnesium bromide at −40° caused a bright orange precipitate to be formed, probably $[Fe(mesityl)_2(PEt_2Ph)_2]$. This complex decomposed very rapidly on attempted isolation.

Factors affecting the Stability of Aryl-cobalt(II) *and -iron*(II) *Derivatives.*—Four-co-ordinate cobalt(II) and iron(II) complexes with monodentate ligands, *e.g.*, $[MX_2(PR_3)_2]$ (M = Co, Fe; X = halogen; PR_3 = tertiary phosphine) usually have high magnetic moments and are considered to be tetrahedral. The diaryl-cobalt(II) and -iron(II) complexes are probably forced into a planar configuration by a combination of electronic (or ligand field) and steric effects. Both tertiary phosphines and aryl groups have large ligand field strengths [13,14] and if these are sufficiently great the planar configuration with the electronic arrangements shown in the Figure would be thermodynamically more stable than the tetrahedral arrangement where the ligand field stabilisation energy (L.F.S.E.) will be small. The tetrahedral iron complexes would have the high-spin arrangement (A) because the ligand field splitting is unlikely to be sufficient to give the low-spin arrangement (B) in tetrahedral complexes of metals of the first transition series.

Possible electronic arrangements of the compounds trans-$[MR_2(PR'_3)_2]$.



The high L.F.S.E. is perhaps the main factor contributing to the stability of organometallic complexes such as described in this series of papers. The large ligand fields ensure a large energy difference (ΔE) between the highest filled electronic energy level and lowest vacant level, as required by our hypothesis to explain the stability of organometallic complexes.[7,9]

If a large ligand splitting were the only factor, all complexes of the type $[MR_2(PR'_3)_2]$ (M = Fe or Co) should be stable, but only those containing aryl groups with two *ortho*-substituents or one bulky *ortho*-substituent are stable. As described when discussing the corresponding nickel compounds,[9] these *ortho*-substituents prevent rotation of the aryl groups about the metal–carbon bond. Thus the aryl groups are fixed with their planes approximately perpendicular to that of the complex and interact specially with the d_{xy}-orbitals by π-bonding, so reducing still further the energy level of d_{xy} and increasing ΔE. This, however, does not appear to be sufficient to account for the stabilities of the iron

[13] Chatt, Gamlen, and Orgel, *J.*, 1959, 1047.
[14] Chatt and Hayter, *J.*, 1961, in the press.

and cobalt complexes, because even one small *ortho*-substituent will prevent rotation but does not give a stable complex; *e.g.*, $[Co(o\text{-tolyl})_2(PEt_2Ph)_2]$ is not stable.

The *ortho*-groups also hinder attack at the metal atom by reagents or solvents.[9] In the nickel series a small *ortho*-substituent, as in the *o*-tolyl complexes, was sufficient to give isolatable derivatives. In the cobalt series a bulky *ortho*-substituent or two smaller *ortho*-substituents were necessary. These will undoubtedly be more effective in hindering attack at the metal atom and they will also tend to stabilise the square planar arrangement of ligands relative to the tetrahedral, owing to the steric repulsions of the *ortho*-substituents. We cannot tell which effect is the more important.

Any formation of the tetrahedral complexes with small L.F.S.E. and ΔE would lead to dissociation of the complex and since the detached alkyl or aryl ligands, unlike most ligands, are not stable entities, this would lead to complete decomposition of the complex. This we consider to be the reason for our inability to prepare the complexes *trans*-[CoX(di-*o*-substituted aryl)$(PEt_2Ph)_2$], where the bulky organic ligand of high ligand field strength has been replaced by a relatively small halogen, X, of low strength, so reducing the stability of the planar configuration relative to the tetrahedral. In nickel complexes of d^8 electronic configuration, which favours the planar arrangement of ligands, complexes of type *trans*-[NiX(*o*-substituted aryl)$(PEt_2Ph)_2$] are stable. In the cobalt series with the d^7 electronic configuration, which is more favourable to a tetrahedral arrangement of ligands, compounds of the above type are unstable.

In the iron(II) complexes with a d^6 electronic configuration the planar arrangement of monodentate ligands is even less likely, and all the factors mentioned above must enter into the stabilisation of *trans*-$[Fe(C_6Cl_5)_2(PEt_2Ph)_2]$. The electronegative chlorine atoms must make an additional important contribution by withdrawing electrons from the metal atom into the aromatic system, so increasing π-bonding and ΔE.

The marked fall in stability along the series *trans*-[M(di-*o*-substituted aryl)$_2(PEt_2Ph)_2$] ($M = Ni > Co > Fe$) may be explained by the progressive reduction, one at a time, in the number of electrons in low-energy orbitals, and corresponding reduction in L.F.S.E. It is unlikely that manganese(II) will form analogous complexes, but chromium(II), which in a planar complex would have four unpaired electrons in low-energy orbitals and a large quantum-mechanical exchange energy, may do so.

The organometallic complexes of iron(II) are particularly interesting because they show that completion of the stable co-ordination shell (octahedral for d^6 complexes) is not essential for stable transition-metal–carbon bonds, and a considerable electron deficiency (in this case, 4 electrons) can be tolerated. The essential features appear to be (*a*) steric shielding of the metal to hinder attack by solvents or reagents, and (*b*) a large ΔE to prevent dissociation. The large ΔE demands ligands of a large ligand field strength and a rectilinear arrangement of ligands as in square-planar or octahedral complexes as opposed to tetrahedral complexes.

Chromium(III), which forms complexes such as $[Cr(CH_2Ph)(H_2O)_5]^{2+}$, is an apparent exception to this.[15] However, so large a ΔE is not necessary here because the three non-bonding *d*-orbitals (d_ϵ) are singly occupied, and so promotion to an antibonding orbital (d_γ) will not be assisted by interelectronic repulsions.

A further point of interest in this series of compounds is the effect of the organic radicals on the attachment of the tertiary phosphine ligands to the metal atom. The compounds $[MCl_2(PR_3)_2]$ (M = Ni, Co) are sufficiently unstable to smell of the phosphine. The organic derivatives have no smell. Evidently the organic groups with their large ligand field splittings so increase L.F.S.E. that the whole complex tightens, stabilising the attachment of phosphorus as well as that of carbon to the metal. In the case of iron(II) this is even more marked; *trans*-$[Fe(C_6Cl_5)_2(PEt_2Ph)_2]$ has no smell, but $[FeCl_2(PEt_2Ph)_x]$ ($x = 2$ or 4) was too labile to be isolated in the presence of air.

[15] Anet and Leblanc, *J. Amer. Chem. Soc.*, 1957, **79**, 2649.

Experimental

M. p.s were determined on a Kofler hot-stage and are corrected. Magnetic moments were measured on the solid compound at 20°.

The tertiary phosphine–cobalt halide complexes were prepared by adding the appropriate phosphine (2 mol.) to a solution of the cobalt halide in ethanol; the complex separated at once or on cooling to 0°.[16] In this way were prepared *dibromobis(triethylphosphine)cobalt*(II), bluish-green prisms, m. p. 134—136° (decomp.) (Found: C, 31·6; H, 7·15. $C_{12}H_{30}Br_2CoP_2$ requires C, 31·5; H, 6·65%), μ 4·5 B.M.; *dichlorobis(diethylphenylphosphine)cobalt*(II), blue needles, m. p. 71—73° (Found: C, 51·95; H, 6·55. $C_{20}H_{30}Cl_2CoP_2$ requires C, 51·8; H, 6·55%); *dibromobis(diethylphenylphosphine)cobalt*(II), bluish-green prisms, m. p. 80—82° (Found: C, 43·6; H, 5·55. $C_{20}H_{30}Br_2CoP_2$ requires C, 43·6; H, 5·5%), μ 4·5 B.M.; *dibromobis(ethyldiphenylphosphine)-cobalt*(II), greenish-blue prisms, m. p. 186—196° (decomp.) (Found: C, 52·2; H, 4·7. $C_{28}H_{30}Br_2CoP_2$ requires C, 51·95; H, 4·65%); *dichlorobis(triphenylphosphine)cobalt*(II), blue prisms, m. p. 247—251° (decomp.) (Found: C, 66·15; H, 4·85. $C_{36}H_{30}Br_2CoP_2$ requires C, 66·05; H, 4·6%), μ 4·3 B.M.; *dibromobis(triphenylphosphine)cobalt*(II), bluish-green prisms, m. p. 234—239° (Found: C, 57·95; H, 4·15. $C_{36}H_{30}Br_2CoP_2$ requires C, 58·15; H, 4·05%); *di-iodobis(triphenylphosphine)cobalt*(II), dark brown prisms, m. p. 209—214° (decomp.) (Found: C, 50·92; H, 3·6. $C_{36}H_{30}CoI_2P_2$ requires C, 51·65; H, 3·6%), μ 4·6 B.M.

Preparation of Arylcobalt(II) *Complexes.*—trans-*Dimesitylbis(diethylphenylphosphine)cobalt*(II) $[Co(mesityl)_2(PEt_2Ph)_2]$. (1) Grignard method. A solution of dibromobis(diethylphenylphosphine)cobalt (6·00 g.) in benzene (50 c.c.) was added at −30° to a solution of mesitylmagnesium bromide, prepared from magnesium (0·96 g.), 2-bromomesitylene (5·9 c.c.), and tetrahydrofuran (20 c.c.). The mixture was allowed to warm and stirred for 40 min. at 20°, then it was cooled to −30° and hydrolysed by dilute hydrochloric acid. Benzene (80 c.c.) was added and the organic layer separated, washed with water, and dried ($MgSO_4$). Evaporation of the solvent and addition of ethanol gave *dimesitylbis(diethylphenylphosphine)cobalt*(II) as lemon-yellow plates (5·25 g.), m. p. 119—124° (decomp.) (from benzene–ethanol) (Found: C, 72·9, 72·9; H, 8·2, 8·7. $C_{38}H_{52}CoP_2$ requires C, 72·5; H, 8·3%), μ 2·5 B.M.

(2) Mesityl-lithium method. A 0·14N-solution of mesityl-lithium in ether (25 c.c.) was added to one of dibromobis(diethylphenylphosphine)cobalt(II) (0·90 g.) in benzene (20 c.c.). After ¾ hr. the mixture was cooled to *ca.* −30° and water was added. The crude product isolated from the organic layer was recrystallised from benzene–methanol–ethanol, to give the desired dimesitylcobalt complex (0·61 g.), identical with that described above.

trans-*Dimesitylbis(triethylphosphine)cobalt*(II). This was similarly prepared in 15% yield from mesitylmagnesium bromide and *trans*-dibromobis(triethylphosphine)cobalt(II). It formed yellow needles, m. p. 113—116° (decomp.), from benzene–ethanol. This compound was very unstable and analytical figures were erratic.

trans-*Di*-(2-*biphenylyl*)*bis(diethylphenylphosphine)cobalt*(II) $[Co(2\text{-}C_6H_4{\cdot}C_6H_5)_2(PEt_2Ph)_2]$. Dibromobis(diethylphenylphosphine)cobalt(II) (3·0 g.) in benzene (50 c.c.) was added at −10° to the Grignard reagent prepared from magnesium (0·48 g.), 2-bromobiphenyl (4·66 g.), and tetrahydrofuran (35 c.c.). The mixture was then stirred at 20° for ¾ hr., cooled to *ca.* −20°, and hydrolysed with dilute hydrobromic acid, and the precipitated solid filtered off and crystallised from benzene–methanol, to give trans-*di*-(2-*biphenylyl*)*bis(diethylphenylphosphine)-cobalt*(II) as yellow prisms (0·73 g.), m. p. 115—119° (decomp.) (Found: C, 75·95; H, 7·15. $C_{44}H_{48}P_2Co$ requires C, 75·75; H, 6·95%), μ 2·6 B.M. A further quantity (0·46 g.) was isolated from the organic layer of the filtrate from the reaction product.

trans-*Di*-(2-*methyl*-1-*naphthyl*)*bis(diethylphenylphosphine)cobalt*(II) $[Co(C_{10}H_6{\cdot}CH_3)_2(PEt_2Ph)_2]$. This *complex* was similarly prepared in 30% yield by using 1-bromo-2-methylnaphthalene to make the Grignard reagent. It was obtained as golden-yellow needles, m. p. 144—146° (much decomp.), from benzene–methanol (Found: C, 74·75; H, 7·25. $C_{42}H_{48}CoP_2$ requires C, 74·85; H, 7·15%), μ 2·7 B.M.

trans-*Bis*(*pentachlorophenyl*)*bis(diethylphenylphosphine)cobalt*(II) $[Co(C_6Cl_5)_2(PEt_2Ph)_2]$. A solution of pentachlorophenylmagnesium chloride was prepared from magnesium (0·48 g.; activated with benzyl chloride, 0·05 g.), tetrahydrofuran (25 c.c.), and hexachlorobenzene

[16] Jensen, *Z. anorg. Chem.*, 1936, **229**, 282.

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(5·7 g.). This Grignard solution was cooled to *ca.* −10°, and dibromobis(diethylphenylphosphine)cobalt(II) (2·5 g.) and ether (15 c.c.) were added. The mixture was then stirred at 20° for 70 min., cooled to *ca.* −30°, and hydrolysed with dilute hydrochloric acid. The resultant precipitate was collected and recrystallised from benzene–methanol, to give *trans-bis(pentachlorophenyl)bis(diethylphenylphosphine)cobalt*(II) as lemon-yellow plates (2·43 g.), m. p. 224—228° (decomp.) (Found: C, 43·55; H, 3·55; Cl, 39·65. $C_{32}H_{30}Cl_{10}CoP_2$ requires C, 43·2; H, 3·4; Cl, 39·85%), μ 2·3 B.M. A further quantity (0·3 g.) was isolated from the mother-liquors of the original reaction mixture.

Preparation of Bis(pentachlorophenyl)bis(diethylphenylphosphine)iron(II).—A solution of the phosphine–ferrous chloride complex was prepared by heating under reflux for 2 hr. a mixture of anhydrous ferrous chloride (0·72 g.), dry benzene (30 c.c.), and diethylphenylphosphine (2·37 g.), cooling, and filtering off the small amount of residue. This solution was then added dropwise at *ca.* −20° to a filtered Grignard reagent, prepared from magnesium (0·96 g.), hexachlorobenzene (11·4 g.), and tetrahydrofuran (30 c.c.). The resultant mixture was then stirred at 20° for 40 min., cooled to −30°, and hydrolysed with dilute hydrochloric acid. The precipitated solid was collected and recrystallised under nitrogen from benzene–ethanol, to give *bis(pentachlorophenyl)bis(diethylphenylphosphine)iron*(II) as golden-yellow prisms (0·13 g.), m. p. 135—142° (decomp.) (Found: C, 43·25; H, 3·55. $C_{32}H_{30}Cl_{10}FeP_2$ requires C, 43·35; H, 3·4%), μ 3·6 B.M.

Dipole moments of some diaryl-cobalt(II) *and -iron*(II) *complexes in benzene at* 25°.

	10^3w	$\Delta E/w$	$10^2\Delta n/w$	$-\Delta v/w$	$_TP$	$_EP$	$_OP$	μ (D)
[Co(mesityl)$_2$(PEt$_2$Ph)$_2$]	7·180	0·491						
	9·392	0·489						
	19·41		12·20					
	26·36		12·23					
	5·369			0·242				
	7·837			0·242	228	210	(−13)	~0
[Co(2-methyl-1-naphthyl)$_2$)(PEt$_2$Ph)$_2$]	5·232	0·591		(0·24)	254 *	(224)	(−3 *)	~0 *
[Co(2-biphenylyl)$_2$(PEt$_2$Ph)$_2$]	3·381	0·550						
	3·436	0·515		(0·53)	258 *	(228)	−4 *	~0 *
[Co(pentachlorophenyl)$_2$(PEt$_2$Ph)$_2$]	2·449	0·488						
	4·055	0·486						
	2·695			0·445				
	3·455			0·463	265 *	(230)	0·8 *	~0 *

* Calculated by using estimated values of densities and refractivities (see Part I of this series [7]).

Determination of Dipole Moments.—These were determined as described in Parts I and II of this series; the measurements and estimated values (shown in parentheses) are recorded in the annexed Table, where the atom polarisation has been assumed to be 15% of the electron polarisation.

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52. *Chromium Phosphates. Part II.*[1] *Phase Diagram at 70° and Further Ion-exchange Studies in the System Chromium(III)–Phosphoric Acid.*

By J. P. Redfern and J. E. Salmon.

A phase-diagram study of the system Cr_2O_3–P_2O_5–H_2O at 70°, where both solutions and solid materials were green, showed that no one solid phase occurred in the range 1—20% of phosphoric oxide. The system gave a series of parallel or slightly diverging tie-lines which are interpreted as indicating that the solid phases possess ion-exchange properties. Preliminary experiments indicate that the material in fact exhibits cation-exchange properties. Batch ion-exchange experiments carried out with solutions aged at 70° indicated the presence of polynuclear cationic complexes. Chromatographic separations employing a gradient elution technique indicated the presence of polynuclear ions having the probable structures $[H_2PO_4\text{–}(Cr\text{–}HPO_4)_n\text{–}Cr\text{–}H_2PO_4]^{z+}$ where $n = 0$, 1, 2, 3, or 6.

In Part I [1] it was shown that at 0° in freshly prepared solutions of the purple tertiary chromium(III) phosphate dissolved in phosphoric acid over a range of 1—25% of phosphoric oxide there was no evidence for complex formation involving the phosphate ion; that is, the ions in such solutions were $[Cr(H_2O)_6]^{3+}$ together with H_3O^+, $H_2PO_4^-$, and HPO_4^{2-}. However, if such solutions were aged at 40° they became green. Ion-exchange and pH studies by Holroyd and Salmon [2] indicated complex formation. Study by Jameson and Salmon [1] of saturated solutions aged at 40° indicated the presence of the following complexes: $[Cr(PO_4)_2]^{3-}$, $[CrHPO_4]^+$, and less probably $[CrH_2PO_4]^{2+}$. It is clear from the difficulty experienced by these workers in achieving a full saturation of the resin that other larger complexes were probably also present: the temperature of 40° was selected as one at which the conversion of the purple-red uncomplexed solution into the green complexed form took place at a reasonable rate. These workers also reported that a radical change seemed to take place in solutions kept above this temperature for any length of time; this was in accord with an observation by Vauquelin.[3] The work has been extended to determine the solubility isotherm of the system at 70° and also the nature of the solid phases and the solution phase at this temperature.

Experimental

Apparatus.—The ageing of solutions at 70° was carried out in an air thermostat. The samples for the phase studies were treated as described in Part I.[1] The solutions for use in the ion-exchange studies were aged in glass bottles closed with Polythene stoppers.

Preparation of Solutions.—Solutions were prepared by dissolving the purple tertiary salt [1] in phosphoric acid solutions and ageing them at 70°. The time required for equilibration was found by an ion-exchange method. At suitable periods an aliquot part of the ageing solution was transferred to a dry, conical flask into which had been introduced ½ g. of the cation-exchanger " ZeoKarb 225 " (20—40 mesh; 8% cross-linked) (H form) or 1 g. of the anion-exchanger DeAcidite FF (20—40 mesh; 8% nominal cross-linking) (PO_4 form). After a period the resin was separated and the sorbed species were eluted and analysed for chromium or phosphate. A plot of the uptake against the time of ageing gave a smooth curve reaching a constant value (either a maximum or minimum), which was taken as the criterion for equilibrium.

Resins.—The strongly acidic monofunctional cation-exchanger " ZeoKarb 225 " was used for both the batch and the column experiments. Resins of varying degrees of cross-linking

[1] Part I, Jameson and Salmon, *J.*, 1955, 360.
[2] Holroyd and Salmon, *J.*, 1956, 269.
[3] Vauquelin, *Ann. Chim. Phys.*, 1798, **25**, 194.

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were employed; the best measure of this was provided by the weight-swelling values, measured by Pepper, Paisley, and Young's centrifuge method.[4]

Batch Experiments.—The technique was that outlined by Jameson and Salmon,[5] modified to permit more efficient elution of the sorbed species after the resin had been transferred to a column. The resin was kept in contact for some considerable time with successive small portions of the eluting agent. This method has the advantage of reducing the amount of eluting agent needed to achieve complete removal of the sorbed species and facilitating subsequent handling and analysis.

Column Experiments.—To the top of the resin column (1 × 35 cm.) was fitted a sintered-glass disc in order to trap any solid particles which could contaminate the resin bed and to prevent the resin particles from flowing into the rest of the apparatus on back-washing. The supply to the column was from a reservoir connected to the column through a mixing chamber, which was stirred magnetically. Concentrations of the solutions in the mixing chamber and the reservoir and the volume of the liquid in the mixing chamber were varied until they gave a clear separation of the complexes on the column. However, a theoretical expression was derived [6] for the exact concentration of the eluant entering the column at a given time t, *viz.*,

$$v_0 \ln [(c_0 - c_1)/(c - c_1)] = c$$

where c = concentration of eluant leaving mixing chamber at time t, c_1 = concentration of solution in the reservoir, c_0 = concentration initially of the solution in the mixing chamber, v = the volume delivered after time t, v_0 = volume of liquid in the mixing chamber (constant throughout experiment). Under the conditions used in the present study, the mixing chamber always contained water initially, *i.e.*, $c_0 = 0$. The equation may be rearranged to give the concentration at time t:

$$c = c_1(e^{v/v_0} - 1)/(e^{v/v_0})$$

Analysis.—Chromium was determined as before; [1] it was shown that nitric acid in the concentrations encountered did not interfere. The phosphate was determined as phosphomolybdate, dried at 110°, and weighed after breakdown of the complexes by treatment with ammonia (*d* 0·880) and a few drops of 100-vol. hydrogen peroxide, acidification, and prolonged boiling.

Results and Discussion

Phase Diagram.—The system was studied at 70° for the range of solutions up to 66% of phosphoric oxide. Samples containing more than 20% were gel-like and separation into solid and liquid phases proved impossible. The results, given in Table 1 and Fig. 1, show little resemblance to those found at 40°.[1] The system of parallel or near-parallel tie-lines could be interpreted in one of the following ways: (i) The system is in

Table 1. *Phase-diagram results of the system* Cr_2O_3–P_2O_5–H_2O *at* 70°.

Solution		Solid		Solution		Solid		Solution		Solid	
Cr_2O_3 (%)	P_2O_5 (%)	Cr_2O_3 (%)	P_2O_5 (%)	Cr_2O_3 (%)	P_2O_5 (%)	Cr_2O_3 (%)	P_2O_5 (%)	Cr_2O_3 (%)	P_2O_5 (%)	Cr_2O_3 (%)	P_2O_5 (%)
0·09	1·07	7·32	9·77	2·39	8·71	10·27	17·65	6·36	14·36	15·50	24·90
0·24	2·24	7·90	11·55	3·28	9·43	7·87	14·70	6·46	14·13	13·25	22·50
0·48	2·90	8·15	12·28	3·17	9·92	13·29	21·73	8·61	17·23	9·76	18·67
1·43	5·37	9·43	15·08	3·92	10·49	—	—	9·09	17·93	17·36	27·72
1·87	6·62	7·75	13·49	5·44	13·18	6·76	14·03				

metastable equilibrium. In the system Fe_2O_3–P_2O_5–H_2O at 25° various workers [7] found similar tie-lines which persisted up to 20% of phosphoric oxide, but it was shown by Jameson and Salmon [8] that such tie-lines were but one of a number of stages that the

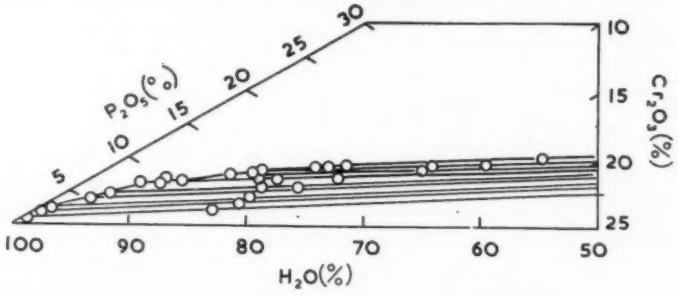
[4] Pepper, Paisley, and Young, *J.*, 1953, 4097.
[5] Jameson and Salmon, *J.*, 1954, 4013.
[6] Ernst and Redfern, unpublished work.
[7] Cameron and Bell, *J. Phys. Chem.*, 1907, **11**, 363; Carter and Hartshorne, *J.*, 1923, **123**, 2223; Salmon, *J.*, 1952, 2316.
[8] Jameson and Salmon, *J.*, 1954, 28.

system went through before stable equilibrium was attained—in the present work care was taken to ensure that equilibrium had been truly attained.

(ii) That solid solutions were being formed between the green tertiary phosphate and one or more acid components. Solid solutions have been classified by Roozeboom [9] and by Ricci [10] as being of six types readily distinguishable by the use of the Roozeboom diagram, in which the percentage of A in the liquid is plotted against that in the solid in contact (the water content being ignored), *i.e.*, 100A/(A + B)%, where A and B are the two salts concerned. Several possibilities for A and B were tried but in no case could the present system be described as being one of the six types.

(iii) That a solid phase Cr_2O_3,P_2O_5,xH_2O has sorbed more or less phosphoric acid according to the composition of the liquid phase; Carter and Hartshorne [7] interpreted

FIG. 1. Cr_2O_3–P_2O_5–H_2O *at* 70°.



the parallel tie-lines in the ferric system in this way. If such adsorption is pictured as purely physical, it presumably depends on the surface area of the solid, and it is difficult to see how this would consistently lead to parallel tie-lines.

(iv) The system is behaving as an ion-exchange material. Jameson and Salmon [8] interpreted the parallel tie-lines in the metastable ferric system as due to the fact that $H_6[Fe(PO_4)_3]$ which separated out initially acted as a cation-exchanger. Recent work [11,12] has shown that some hydrous oxides of ter- and quadri-valent metals show weakly basic anion-exchange properties, and that some phosphates and tungstates behave in a similar fashion as weakly acid-cation exchangers. No investigation of the structure has yet appeared, but it was suggested that the solid material consisted (*e.g.*, in the case of the zirconium phosphate) of zirconium atoms linked by bridging oxygen atoms: to the zirconium atoms, acid phosphate groups were attached and these had replaceable hydrogen ions for cation exchange.[12] The material in the present system was examined for possible ion-exchange properties. Solid material, isolated from the mixture used for the phase diagram at 70°, was loaded into a small column (1 × 10 cm.). Two such samples were treated with a dilute solution of chrome alum. Sample 1 sorbed 0·014 mmole of $[Cr(H_2O)_6]^{3+}$, and sample 2 0·046 mmole. In both cases it was shown that the solution became more acid on passage through the material. Subsequently, sample 2 was treated with a dilute solution of nitric acid (pH 1·5) and $[Cr(H_2O)_6]^{3+}$ ions were desorbed. The same sample was then treated with 0·1M-sodium chloride, and hydrogen ions were desorbed. All effluents from the two samples (about 0·5 g. dry weight) were checked for phosphate and in every case none was detected. In the light of this, and in view of the predominance of complex cations present in solutions in equilibrium with the solid material as shown by

[9] Roozeboom, *Z. phys. Chem.*, 1891, **8**, 521.
[10] Ricci, *J. Amer. Chem. Soc.*, 1935, **57**, 805.
[11] Kraus and Phillips, *J. Amer. Chem. Soc.*, 1956, **78**, 249, 694; Amphlett, McDonald, and Redman, *Chem. and Ind.*, 1956, 1314; 1957, 365; Anderson, *Trans. Faraday Soc.*, 1958, **54**, 130.
[12] Amphlett, McDonald, and Redman, *J. Inorg. Nuclear Chem.*, 1958, **6**, 220, 236.

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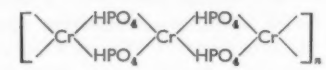
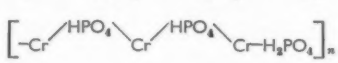
the present studies, it is to be expected that the solid material consists of a polymeric network of one or a combination of both of the following types:

Type 1 

Type 2 

Ion-exchange.—Jameson and Salmon [1] commented on the care that is needed in interpretation of the batch ion-exchange studies at 40° owing to several factors, *viz.*, the size of the complexes being sorbed, the time of ageing of the solution, and the time of contact of the solution with the resin. In all the present work fully aged solutions were used and the other two factors were investigated. If some steric factor is involved, the

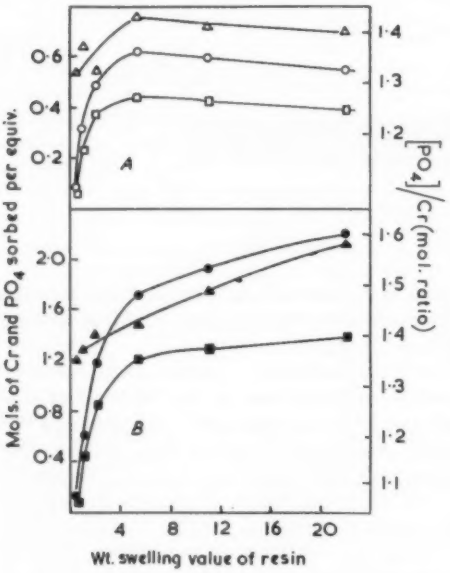


FIG. 2. *Sorption on ZeoKarb 225 (H form) from solutions aged at 70° for 4 days.*

(A) Solution contained 2·5% of P_2O_5 and 0·3% of Cr_2O_3.

PO_4 *sorbed.* □ Cr *sorbed.* Δ $[PO_4]/[Cr]$ *mole ratio species sorbed.*

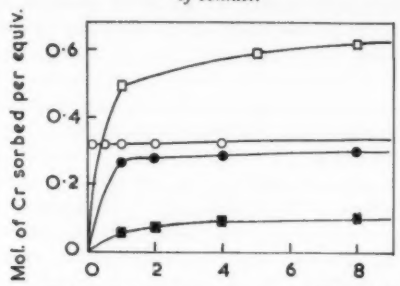
(B) Solution contained 12·5% of P_2O_5 and 5·0% of Cr_2O_3.

● PO_4 *sorbed.* ■ Cr *sorbed.* ▲ $[PO_4]/[Cr]$ *mole ratio species sorbed.*

In every case resin and solution were in contact for 2 hours.

use of resins of various degrees of cross-linking should reflect the size of the complex ions being sorbed, in that tightly cross-linked (low weight-swelling) resins should preclude the entry of large ions. A range of solutions and resins of varying weight-swelling values being used, there was a marked fall in the amount of chromium and phosphate sorbed per equivalent of exchanger as the resin became more tightly cross-linked (see Fig. 2). The mole ratio PO_4 : Cr also varied. Thus it appeared likely that a number of complexes competed for the exchange sites on the resin and that some of these were of considerable size. Increasing the time of contact of the solution with the resin caused a gradual rise in the amount of chromium and phosphate sorbed, especially for the medium cross-linked resins. In Fig. 3 this is compared with the rapid sorption of $[Cr(H_2O)_6]^{3+}$ from unaged solutions by the same resin. The shape of the curve for the uptake of the complexes indicates that the ions being sorbed are large and that entry is slow. It is also possible that the ions being sorbed undergo chemical attack on contact with the, initially, strongly acid media of the resin at room temperature, and that these smaller fragments are subsequently sorbed on the resin. The possibility that a number of complexes of similar type

FIG. 3. *Sorption of* Cr *by ZeoKarb* 225 (H *form) from fresh and aged solutions after various times of contact.*



Weight-swelling value of resin	Moles/equiv. Cr sorbed	Condition of solution
1·98	○	Fresh
	□	Aged at 70° for 4 days
0·43	●	Fresh
	■	Aged at 70° for 4 days

Solution contained 5·0% *of* P_2O_5 *and* 1·0% *of* Cr_2O_3.

TABLE 2. *Ion-exchange chromatography: gradient elution of chromium*(III) *complexes in solutions of constant* P_2O_5 *concentration, after ageing at* 70°.

Solution Cr (*m*)	Solution PO_4 (*m*)	Complexes in order of elution	v_0 (ml.)	c_1 NH_4NO_3 (N)	c_1 HNO_3 (N)	Cr found (mmole)	PO_4 found (mmole)	Cr : PO_4 mole ratio	Probable ideal Cr : PO_4 mole ratio
0·039	2·113	A	550	1·00	—	0·054	0·109	1 : 2·02	1 : 2
0·196	2·113	A	575	0·66	—	0·196	0·406	1 : 2·07	1 : 2
		B		0·66	—	0·077	0·111	1 : 1·45	1 : 1·5
		C		0·66	—	0·065	0·088	1 : 1·36	1 : 1·33
0·392	2·113	A	580	0·66	—	0·182	0·364	1 : 2·00	1 : 2
		B		0·66	—	0·138	0·201	1 : 1·46	1 : 1·5
		C		0·66	—	0·112	0·156	1 : 1·38	1 : 1·33
		D		0·66	4	0·049	0·060	1 : 1·22	1 : 1·25
		G		—	8	0·101	0·051	1·99 : 1	2 : 1
0·588	2·113	A	580	0·66	—	0·073	0·179	1 : 2·47	1 : 2
		B		0·66	—	0·071	0·102	1 : 1·45	1 : 1·5
		C		0·66	—	0·038	0·050	1 : 1·33	1 : 1·33
		D		0·66	4	0·106	—	1 : 1·25 *	1 : 1·25
		E		0·66	4	0·144	0·160	1 : 1·12	1 : 1·125
		F		0·66	4	0·150	0·152	1 : 1·01	1 : 1
0·784	2·113	A	580	0·66	—	0·032	0·064	1 : 1·99	1 : 2
		B		0·66	—	0·087	0·140	1 : 1·61	1 : 1·5
		C		0·66	—	0·026	0·035	1 : 1·33	1 : 1·33
		D		0·66	4		Not detected		
		E		0·66	4	0·258	0·295	1 : 1·14	1 : 1·125
		F		0·66	4	0·177	0·178	1 : 1·00	1 : 1

2% Cross-linked ZeoKarb 225 (50—100 mesh) (H form) was contained in a column 1·2 × 33 cm. The results are given only on the main portion of the eluted complex: 0·5 g. samples of the resin were shaken with 10 g. of the fully aged solution for 2 hr., washed free from phosphate on a sintered-glass filter, and loaded on to the top of the prepared column. v_0 and c_1 have the significance given in the text.

* By inference; also indicated in some preliminary chromatographic work. Probable structures that may be assigned to the complexes:

A = $[H_2PO_4{-}Cr{-}H_2PO_4]^+$; B = $[H_2PO_4{-}Cr{-}HPO_4{-}Cr{-}H_2PO_4]^{3+}$; C = $[H_2PO_4{-}Cr{-}(HPO_4{-}Cr)_2{-}H_2PO_4]^{3+}$;
D = $[H_2PO_4{-}Cr{-}(HPO_4{-}Cr)_3{-}H_2PO_4]^{4+}$; E = $[H_2PO_4{-}Cr{-}(HPO_4{-}Cr)_6{-}H_2PO_4]^{7+}$;
F = $[H_2PO_4{-}Cr{-}HPO_4{-}Cr]^{3+}$; G = $[Cr{-}HPO_4{-}Cr]^{4+}$

In complexes B, C, D, and E the charge may be reduced by one or two units by the loss of a H^+ ion from one or both of the terminal phosphate groups, and by more units of charge if hydrogen ions are lost from the bridging phosphate groups.

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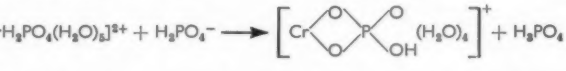
exists in solution, taken together with the likelihood of breakdown, makes it difficult to interpret the results of the batch studies in terms of possible complexes by Salmon's approach.[13] However, the complexes were sufficiently stable for separation chromatographically. Batch desorption and column studies were carried out to determine a suitable eluting agent. Some of the complexes were susceptible to breakdown by H^+ ions, and hence chromatographic development was initially by ammonium nitrate and later by a mixture of nitric acid and ammonium nitrate. The results are given in Table 2. The structures of A and G must be $[H_2PO_4–Cr–H_2PO_4]^+$ and $[Cr–HPO_4–Cr]^{4+}$ or $[Cr–PO_4–Cr]^{3+}$, and presumably the other complexes must be intermediate in character and in charge.

The major difference between the chromium(III)–phosphoric acid system at 0—40° and at 70° is the appearance of polynuclear complexes and the parallel tie-lines in the phase-diagram study, neither of which has been noted in the previous work.[1] This may be accounted for by the fact that phosphoric acid is a weaker acid at higher temperatures. Thus by applying Harned and Embree's equation [14] for the temperature-dependence of the ionisation constants of weak acids to phosphoric acid, it may be seen that K_1 and K_2 are decreasing above 43·1° (see Nims [15]). Thus it is clear that above this temperature a somewhat different situation exists in the system. The following mechanism for the formation of complexes is likely:

Step 1: $[Cr(H_2O)_6]^{3-} \longrightarrow [Cr(H_2O)_5]^+$ (see ref. 16)

Step 2: $[Cr(H_2O)_5]^{3+} + H_2PO_4^- \xrightarrow{\text{rapid}} [CrH_2PO_4(H_2O)_5]^{2+}$

Step 3*a*: $[CrH_2PO_4(H_2O)_5]^{2+} + H_2PO_4^- \longrightarrow [Cr(H_2PO_4)_2(H_2O)_4]^+$

or Step 3*b*: $[CrH_2PO_4(H_2O)_5]^{2+} + H_2PO_4^- \longrightarrow$  $+ H_3PO_4$

Both steps 3*a* and 3*b* involve the loss of a second molecule of water from the chromium cation. Presumably 3*a* will be favoured in the present system since the formation of a stable four-membered ring depends, amongst other factors, on the radius of the unhydrated metal ion. The importance of this radius was established by Genge and Salmon [17] for phosphato-complexes of the tervalent metals which use $sp^3d_{\gamma}^2$-hybrid orbitals. They also showed that for an unhydrated metal ion a radius of 0·72 Å was the optimum for a ring of least strain. The experimental results were in accord with this deduction for metals using such hybrid orbitals. The authors pointed out, however, that their studies did not extend to those metals in which inner *d*-orbitals would probably be employed, *i.e.*, in $d_{\gamma}^2sp^3$-hybrid orbitals. Chromium(III), although similar to iron(III) in its ionic radius, more often resembles cobalt rather than iron, aluminium, gallium, and the tervalent rare earths, and it is likely that inner *d*-orbitals are employed by chromium and cobalt. Daniel and Salmon [18] prepared a phosphatotetramminecobalt(III) complex in which one PO_4 chelate ring, but no bis-chelate compound, appeared to be formed. Hence with cobalt(III) and possibly with chromium(III), only one four-membered ring, at most, can be formed with phosphate.

Most of the chromium complexes found in aged solutions of chromium(III) in phosphoric acid are cationic, having a PO_4 : Cr mole ratio of x : 1 where $x > 1$, which implies that the phosphato-groups must have more than one associated hydrogen atom. This precludes the formation of chelate rings. Thus, on several counts, it seems unlikely that step 3*b* makes an important contribution to the overall equilibrium and it is probable that step 3*a*

[13] Salmon, *Rev. Pure Appl. Chem.*, 1956, **6**, 24.
[14] Harned and Embree, *J. Amer. Chem. Soc.*, 1934, **56**, 1050.
[15] Nims, *J. Amer. Chem. Soc.*, 1934, **56**, 1110.
[16] Plane and Taube, *J. Phys. Chem.*, 1952, **56**, 33.
[17] Genge and Salmon, *J.*, 1959, 1459.
[18] Daniel and Salmon, *J.*, 1957, 4207.

is favoured. Further complexes may then be formed by suitable elimination reactions of the type:

$$[H_2PO_4{-}Cr{-}H_2PO_4]^+ + [H_2PO_4{-}Cr{-}H_2PO_4]^+ \longrightarrow [H_2PO_4{-}Cr{-}HPO_4{-}Cr{-}H_2PO_4]^{2+} + H_3PO_4$$

This is similar to that elimination reaction described by Bjerrum [19] in the process of the formation of polynuclear complexes of chromium involving hydroxyl bridging and referred to as " olation."

BATTERSEA COLLEGE OF TECHNOLOGY, LONDON, S.W.11. [*Received, March 30th*, 1960.]

[19] Bjerrum, *Z. phys. Chem.*, 1907, **59**, 336.

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53. *Aromatic Reactivity. Part XII.*[1] *Cleavage of Aryltriethylgermanes by Aqueous-methanolic Perchloric Acid.*

By C. EABORN and K. C. PANDE.

We have measured spectrophotometrically the rates of cleavage of a large number of aryltriethylgermanes in a mixture of aqueous perchloric acid and methanol. The results provide a detailed picture of substituent effects in an electrophilic aromatic substitution. These effects are discussed, and compared with those in other electrophilic aromatic substitutions.

There is a precise linear free-energy relationship between the rates of cleavage of aryltriethylgermanes and those of the analogous aryltrimethylsilanes.

WE have measured the rates of cleavage at 50·0° of a number of aryltriethylgermanes (mainly monosubstituted phenyltriethylgermanes) by a mixture of 2 volumes of aqueous perchloric acid and 5 volumes of methanol:

$$Ar{\cdot}GeEt_3 + HOX \xrightarrow{H^+} ArH + Et_3Ge{\cdot}OX \quad (X = H \text{ or } Me)$$

The reaction, aromatic protodetriethylgermylation (here referred to for brevity as degermylation—cf. ref. 2), is analogous to the cleavage of aryltrimethylsilanes (desilylation) previously described.[2,3] Both reactions are electrophilic aromatic substitutions, and the influence of the constitution of the aryl group on the ease of cleavage provides additional information on substituent effects in such substitutions.

The near-ultraviolet absorption spectrum of an $Ar{\cdot}GeEt_3$ compound is shifted towards the visible region compared with that of the parent ArH compound (as with the corresponding $Ar{\cdot}SiMe_3$ compound); there is little difference in shapes of the spectra. By suitable choice of wavelength it is possible to measure the rate of cleavage of the aryltriethylgermanes in aqueous-methanolic perchloric acid by the spectrophotometric technique used for the aryltrimethylsilanes.[2,3]

The results are shown in Table 1 as first-order rate constants, k_1, observed at specified concentrations of acid, and also as rates, k_{rel}, relative to the rate of reaction of the parent compound, phenyltriethylgermane. It must be stressed that the spread of rates is such that all the compounds cannot accurately be studied at the same concentration of acid, and some values of k_{rel} are obtained by the overlap procedure used with silicon compounds.[2,3] Since the medium employed consists of 4 volumes of aqueous perchloric acid mixed with 10 volumes of methanol, its water content changes somewhat as the concentration of the acid is varied, and the values of k_{rel} might be different if all the compounds

[1] Part XI, Eaborn and Taylor, *J.*, 1960, 3301.
[2] Eaborn, *J.*, 1956, 4858.
[3] Deans and Eaborn, *J.*, 1959, 2299.

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were examined in one medium, but we believe this effect to be small. It can be seen from Table 1 that where k_{rel} was determined for a compound at two acid concentrations the difference in the values was small, and was also random over the range of compounds so studied.

The results form the most detailed pattern of substituent effects yet obtained for an electrophilic aromatic substitution under one set of conditions. (More substituents have been studied in desilylation,[2,3] but only by carrying out some of the measurements in acetic acid–sulphuric acid–water.) Qualitative examination of the results reveals the following features:

(i) Activation by *p*-alkyl groups is in the Baker–Nathan order Me > Et > Pr^i > Bu^t, and by *m*-alkyl groups is in the inductive order Bu^t > Me. The Baker–Nathan order has been observed so far for *para*-groups in all electrophilic aromatic substitutions except nitration in aqueous acetic acid [4] and aromatic hydrogen exchange in some media;[5] the

TABLE 1. *Cleavage of substituted phenyltriethylgermanes by a mixture of aqueous perchloric acid* (2 *vol.*) *and methanol* (5 *vol.*) *at* 50·0°.

No.	Substituent	[HClO$_4$] [a] (M)	10^3k_1 (min.$^{-1}$)	k_{rel}	No.	Substituent	[HClO$_4$] [a] (M)	10^3k_1 (min.$^{-1}$)	k_{rel}
1	*p*-NMe$_2$	0·00527	81·3	—	11	*p*-Pr^i	6·21	78·8	12·0
		0·0527	99·5	—	12	*p*-Bu^t	6·21	75·1	11·5
		0·229	100·4	—	13	*o*-Ph	7·34	33·4	3·22
				ca.	14	*p*-Ph	7·34	27·9	2·69
				3 × 10^6	15	2,3-C$_4$H$_4$ [c]	7·34	64·1	6·2
2	2,4,6-Me$_3$ [b]	0·0527	37·3	—	16	3,4-C$_4$H$_4$ [d]	9·15	49·3	1·79
		0·229	179	13,600	17	*m*-Bu^t	7·34	35·2	3·2
3	*p*-OH	0·229	36·0	2,730			9·15	87·3	3·4
		0·495	88·0	—	18	*m*-Me	7·34	22·2	2·14
4	*p*-OMe	0·495	17·4	540			9·15	57·6	2·08
		0·970	45·2	—	19	H	4·01	1·54	1
5	*o*-OMe	0·970	17·5	—			6·21	6·55	1
		2·80	129	207			7·34	10·36	1
6	*p*-CH$_2$·SiMe$_3$	0·970	13·3	—			9·15	27·6	1
		2·80	101·5	162	20	*p*-F	7·34	9·2	0·96
7	*p*-OPh	2·80	24·5	39			9·15	26·4	0·89
		4·01	53·0	34·5	21	*m*-MeO	7·34	5·97	0·57
8	*p*-Me	2·80	8·8	—			9·15	16·1	0·58
		6·21	91·3	(13·9)	22	*p*-Cl	9·15	4·60	0·167
		7·34	148	14·1			11·91	21·2	—
9	*o*-Me	2·80	7·69	12·3	23	*p*-Br	9·15	3·42	0·124
		4·01	19·2	12·5			11·91	16·5	0·130
		6·21	76·9	—	24	*p*-I	11·91	16·7	0·131
10	*p*-Et	6·21	85·1	13·0	25	*m*-Cl	11·91	2·09	0·0165

[a] Concn. of the aqueous perchloric acid. [b] Denotes mesityltriethylgermane. [c] Denotes 1-naphthyltriethylgermane. [d] Denotes 2-naphthyltriethylgermane.

inductive order has, as far as we are aware, been observed for *m*-Me and *m*-Bu^t groups in all the electrophilic aromatic substitutions studied.[5,6]

(ii) *para*-Halogen is deactivating in the order *p*-I ≃ *p*-Br > *p*-Cl > *p*-F, as in desilylation.[2,3] The *p*-fluoro-group is deactivating (though very slightly) as it is in proto- and bromo-desilylation [2,3,7] and in nitration,[8] but contrary to its effect in molecular chlorination in acetic acid,[9] and in detritiation.[5] It seems that in reactions of high electron demand (as measured, for example, by the influence of a *p*-methyl group) the +*E* effect of the fluorine atom overpowers the −*I* effect. The anomaly remains, however, that the

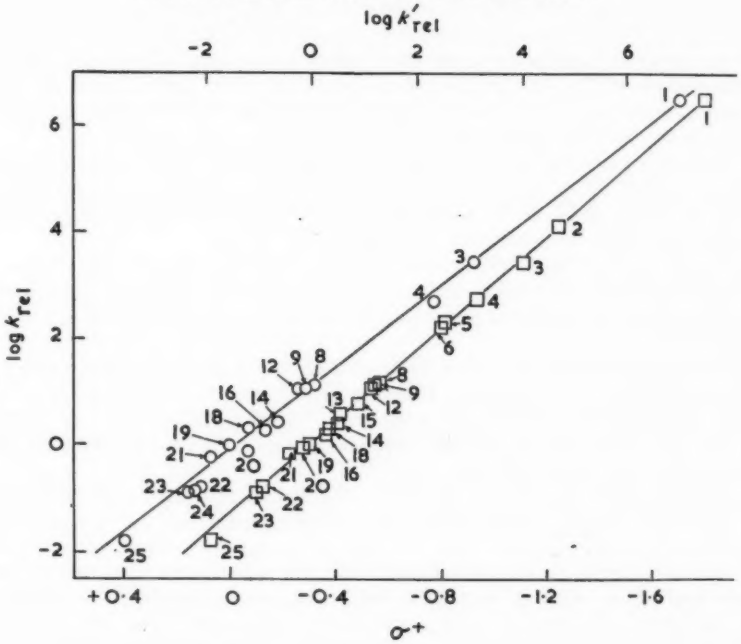
[4] Cohn, Hughes, Jones, and Peeling, *Nature*, 1952, **169**, 291.
[5] Eaborn and Taylor, *Chem. and Ind.*, 1959, 949.
[6] Stock and Brown, *J. Amer. Chem. Soc.*, 1959, **81**, 5621.
[7] Eaborn and Webster, *J.*, 1957, 4449; *J.*, 1960, 179.
[8] de la Mare and Ridd, "Aromatic Substitution, Nitration and Halogenation," Butterworths Scientific Publ., London, 1959, p. 85.
[9] de la Mare, *J.*, 1954, 4450.

p-fluoro-group can deactivate in nucleophilic aromatic substitution,[10] where the $+E$ effect cannot be called into operation.

(iii) The methoxy-group activates more from the *para*- than from the *ortho*-position, and deactivates from the *meta*-position. Deactivation by the *m*-methoxy-group appears to be the common result in electrophilic aromatic substitution, but the group is reported to be activating in molecular bromination in acetic acid.[11]

(iv) The *p*-phenoxy-group activates much less effectively than the *p*-methoxy-group. This effect has been observed previously for molecular bromination in acetic acid,[9] and almost certainly operates in nitration in acetic anhydride, in which the *p*-phenoxy-group activates only 234 times.[12] The smaller effect of the *p*-phenoxy-group presumably results partly from the $-I$ effect of the phenyl group, partly from increased steric interaction

Plot of $\log k_{rel}$ *against* (□) $\log k'_{rel}$ *and against* (○) σ^+.



between the group and the hydrogen atoms *ortho* to it, which prevents the phenoxy-group from getting into the plane of the ring and thus hinders p_π–p_π overlap, and partly from conjugation of π-electrons of the oxygen atom with the phenyl group, which renders them less available to activate the ring in which substitution is occurring.

(v) The phenyl group activates the *ortho*- more than the *para*-position, as in protodesilylation but not bromodesilylation.[13] The 4-position of biphenyl is more reactive in degermylation than is the 2-position of naphthalene, as in other electrophilic substitutions except possibly nitration (cf. ref. 14).

[10] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons, Ltd., London, 1953, p. 805; Miller, *Austral. J. Chem.*, 1956, **9**, 61.
[11] de la Mare and Vernon, *J.*, 1951, 1764.
[12] Dewar and Urch, *J.*, 1958, 3079.
[13] Deans, Eaborn, and Webster, *J.*, 1959, 3031.
[14] Eaborn, Lasocki, and Webster, *J.*, 1959, 3034.

(vi) The effect of any substituent is smaller in protodegermylation than in protodesilylation. This is to be associated with the higher reactivity of the aryl–germanium bond than of the aryl–silicon bond, which means that there is less demand on the electrons of the aryl system on going from the ground state to the transition state.

More quantitative analysis of the results in Table 1 reveals the following features:

(vii) The plot of log k_{rel} against log k'_{rel}, where k'_{rel} refers to acid cleavage of aryltrimethylsilanes,[2,3,14,15] is an excellent straight line over the whole range of substituents studied (see Figure). The excellence of the plot seems to confirm the accuracy of the experimental data in both desilylation and degermylation, and to justify the overlap procedure used in deducing relative rates. It also supports previous indications that the same mechanism operates in both reactions, with another mechanism possibly operating in destannylation and deplumbylation.[15]

(viii) The free-energy relationship noticed under (vii) holds exactly even for the *ortho*-substituted compounds, including the mesityl compounds, even though there is thought to be steric acceleration of the desilylation in this case.[16] It appears that, coincidentally, the Et_3Ge group has exactly the same steric effect in degermylation as the Me_3Si group has in desilylation. (The size of the groups is not the only factor here: the extent to which the configuration at the central carbon approaches tetrahedral in the rate-determining transition state is also important.)

(ix) When the values of k_{rel} are expressed as rate factors f, the ratio $(\log f_p^{Me})/(\log f_m^{Me})$ has a value of 3·57. This compares with a value of 3·66 in desilylation, and falls in the middle of the range, 3·18—4·72, which covers a large number of electrophilic aromatic substitutions for which accurate data are available.[17]

The ratio $(\log f_p^{But})/(\log f_m^{But})$ has a value of 2·05. This compares with a value of 2·27 for protodesilylation in hydrogen chloride–acetic acid–water, and falls just outside the range of 2·27—3·82 which covers nine electrophilic aromatic substitutions for which data are available.[6]

The ratio $(\log f_p^{Me})/(\log f_p^{Ph})$ has a value of 2·73, which compares with a value of 2·82 for protodesilylation of aryltrimethylsilanes in acetic acid–sulphuric acid–water.[13] This ratio shows considerable variation over the range of reactions for which it is accurately known, the $+E$ effect of the phenyl group being more effective in reactions of large electron demand (*i.e.*, with large values of f_p^{Me}).[13]

The ratio $(\log f_p^{Me})/(\log f_\beta^{C_4H_4})$ has a value of 4·54, compared with 3·96 in protodesilylation. This ratio varies considerably for the few reactions for which it can be calculated.[14]

(x) The substituent effects correlate well with the substituent constants σ^+ proposed by Brown and his co-workers for electrophilic aromatic substitutions, as shown by the straight-line plot (see Figure) of log k_{rel} against σ^+. (The slope, ρ, is 3·9.) Those points which lie furthest from the line refer to substituents (*p*-Ph, *p*-halogens, and 3,4-C_4H_4) to which, it has been argued,[2,13,14] single satisfactory σ^+ substituent constants cannot be assigned.

Since substituent effects in protodegermylation correlate so well with those in protodesilylation, it follows that other, more complex, approaches to the use of substituent constants which have been applied successfully to the desilylation [19] would have the same success with degermylation.

Two features of the experimental work should be noted. First, the cleavage of the compound *p*-$NMe_2{\cdot}C_6H_4{\cdot}GeEt_3$ is much slower than would be expected from the value of

[15] Eaborn and Pande, *J.*, 1960, 1566.
[16] Eaborn and Moore, *J.*, 1959, 3640.
[17] Stock and Brown, *J. Amer. Chem. Soc.*, 1959, 3323.
[18] Brown and Okamoto, *J. Amer. Chem. Soc.*, 1958, 4979, and references therein.
[19] Deno and Evans, *J. Amer. Chem. Soc.*, 1957, **79**, 5804; Yukawa and Tsuno, *Bull. Chem. Soc. Japan*, 1959, **32**, 971; McNulty and Pearson, *J. Amer. Chem. Soc.*, 1959, **81**, 612; see also Bekhum, Verkade, and Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.

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k_{rel} given in Table 1, because the compound is almost all converted into the unreactive salt, p-$HMe_2\overset{+}{N}\cdot C_6H_4\cdot GeEt_3$, in the media used. The rate of cleavage is fairly insensitive to the acid concentration, except for very low concentrations, as with the analogous trimethylsilyl compound.[2] The value of k_{rel} for the free base is derived, as in desilylation,[2] in the following way: p-dimethylaminophenyltriethylgermane reacts at an 0·00527M(added)-acid concentration 2·2 times as fast as the mesityl compound does in 0·0527M(added)-acid, and so about 22 times as fast as the mesityl compound would react in the weaker acid. In the reaction involving 0·00527M(added)-acid, 11·0% of *NN*-dimethylaniline is found spectrophotometrically to be present as free base, and, since the p-triethylgermyl derivative probably has a rather similar base strength, about 11% of it will remain as free amine. Thus p-dimethylaminophenyltriethylgermane is about 22×9 times as reactive as the mesityl compound, and thus about 3×10^6 times as reactive as phenyltriethylgermane.

Secondly, the phenol p-$HO\cdot C_6H_4\cdot GeEt_3$ could not be obtained satisfactorily pure: consequently the compound p-$Me_3Si\cdot O\cdot C_6H_4\cdot GeEt_3$ was used, since it was known that this would solvolyse very rapidly in the cleavage medium to give the phenol, the cleavage of which could then be studied. In confirmation, cleavage was found to proceed at an identical rate for the compounds p-$Me_3Si\cdot O\cdot C_6H_4\cdot SiMe_3$ and p-$HO\cdot C_6H_4\cdot SiMe_3$.

Experimental

Materials.—The preparation and properties of the aryltriethylgermanes have been described.[20]

Table 2.

X	Concn. (M)	λ (mμ)	X	Concn. (M)	λ (mμ)
H	6×10^{-3}	266	*o*-Ph	$5{\cdot}5 \times 10^{-4}$	280
o-Me	$5{\cdot}5 \times 10^{-3}$	276	*p*-Ph	6×10^{-5}	275
m-Me	6×10^{-3}	275, 276	*o*-OMe	$5{\cdot}5 \times 10^{-4}$	283, 287
p-Me	$5{\cdot}5 \times 10^{-3}$	273	*m*-OMe	11×10^{-4}	286
p-Et	6×10^{-3}	276	*p*-OMe	$10{\cdot}5 \times 10^{-4}$	281, 283
p-Pr^i	4×10^{-3}	236, 270	*p*-OPh	4×10^{-4}	251
m-Bu^t	$6{\cdot}5 \times 10^{-3}$	270	*p*-O·SiMe$_3$	$1{\cdot}5 \times 10^{-3}$	240
p-Bu^t	$4{\cdot}5 \times 10^{-3}$	238, 270	*p*-CH$_2$·SiMe$_3$	2×10^{-3}	247
p-F	8×10^{-3}	276	*p*-NMe$_2$	8×10^{-3}	275 [a]
m-Cl	6×10^{-3}	279	,,	8×10^{-4}	275 [b]
p-Cl	5×10^{-3}	277	2,3-C_4H_4	$6{\cdot}4 \times 10^{-4}$	299
p-Br	5×10^{-3}	274	3,4-C_4H_4	$6{\cdot}4 \times 10^{-4}$	294
p-I	6×10^{-3}	288	2,4,6-Me$_3$ [c]	$2{\cdot}5 \times 10^{-3}$	242

[a] $[HClO_4] = 0{\cdot}00527$. [b] $[HClO_4] = 0{\cdot}0527$. [c] Refers to mesityltriethylgermane.

Medium.—The medium was the same as that used in protodesilylation.[2,14] Four vol. of aqueous perchloric acid, of concentration shown in Table 1, were mixed with 10 vol. of a methanolic solution of the organogermane, $X\cdot C_6H_4\cdot GeEt_3$, of concentration shown in Table 2.

Kinetic Methods.—The methods described for protodesilylation were used.[2,14,15] The change in absorption in 1 cm. cells held at 50·0° ± 0·04° was recorded at the wave lengths, λ, shown in Table 2. In the case of the *m*-Cl compound, sealed tubes were used for the reaction samples (for the *p*-Cl and *p*-Br compounds it was shown that runs in cells and sealed tubes gave rate constants agreeing within ±1%). In all cases rate constants of duplicates agreed within 2%.

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The University, Leicester. [*Received, May 19th*, 1960.]

[20] Eaborn and Pande, *J.*, 1960, 3200.

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54. *Catalysis with Evaporated Metal Films in a Flow System. Part I. The Hydrogenation of Benzene and Cyclohexene over Nickel.*

By W. F. Madden and C. Kemball

An apparatus has been developed which keeps metal films free from contamination to an extent sufficient to maintain constant catalytic activity when reactions are followed for 3—4 hr. in a flow system.

Hydrogenation of benzene over nickel films was studied between 0° and 50°, with results in general agreement with those obtained in a static system.[1] Hydrogenation of cyclohexene is 200 times faster than that of benzene at −34°, and the divergence increases with temperature.

Absolute-rate theory confirms that for benzene the slow step is the formation of adsorbed C_6H_8 but it does not distinguish between the three possible mechanisms, (*a*) reaction of gaseous hydrogen with adsorbed benzene, (*b*) simultaneous addition of two chemisorbed hydrogen atoms, or (*c*) reaction between a hydrogen atom and chemisorbed C_6H_7.

It is often difficult to follow a catalytic reaction involving gaseous reactants over evaporated metal films in a static system when the pressure of one of the reactants has to be kept below a comparatively small condensation pressure. Apart from the experimental difficulties in following the disappearance of a low pressure of the reactant or the formation of a low pressure of product, the reaction may be complete in a short time owing to the high activity of this type of catalyst. Reduction of the amount of catalyst is unsatisfactory because of the likelihood of contamination of the smaller surface of a light film as it is prepared. Reduction of the temperature aggravates the problem of following the reaction at increasingly low pressures and may even increase the *percentage* rate of reaction. The latter complication will occur when the activation energy of the reaction is lower than the latent heat of vaporisation (or sublimation) of the least volatile reactant and when the order of reaction with respect to this reactant is zero or negative. Thus, it seemed desirable to develop a technique for the use of evaporated metal catalysts in a flow system, in order to control the rate of reaction by reducing the time of contact between the reactants and the catalyst surface.

Hydrogenation of benzene vapour over nickel was selected as a suitable reaction by which the apparatus might be tested, because reliable data have been obtained for this reaction in a static system by Beeck and Ritchie.[1] At the same time, it seemed important to compare the rates of hydrogenation of cyclohexene and benzene under similar conditions. Smith and Meriwether [2] found that cyclohexene was hydrogenated 8 times faster than benzene when the reactions were carried out in the liquid phase, using solutions in acetic acid, over a bulk platinum catalyst. However, the activation energy for the hydrogenation of cyclohexene was only 2·4 kcal./mole and thus it is possible that diffusion in the liquid phase may have limited the rate of reaction under their conditions. Other evidence, *e.g.*, Anderson's result [3] that cyclohexene is hydrogenated in less than 1 min. on an evaporated nickel catalyst at 0°, suggested that the cycloalkene is hydrogenated much more rapidly than the aromatic molecule. It was considered that a comparison of the kinetic data for the hydrogenation of cyclohexene and benzene with rates calculated by the transition-state theory might assist in the determination of the mechanism of the two reactions.

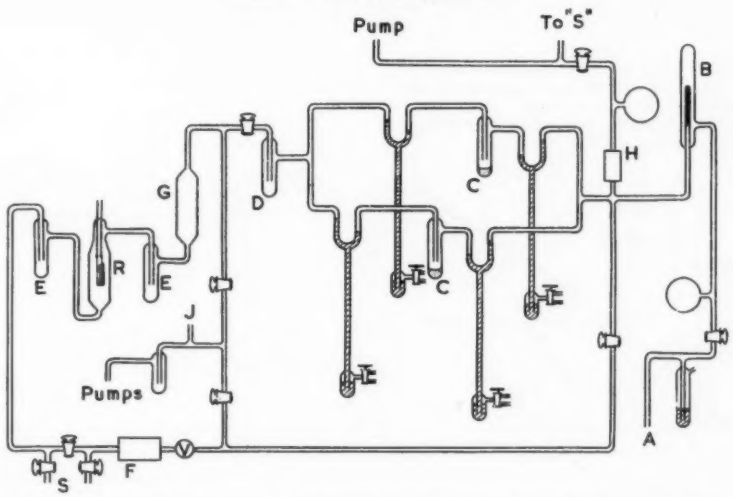
Experimental

As a number of precautions were necessary to avoid contamination of the catalyst during each experiment, a detailed diagram of the apparatus is shown in Fig. 1. Hydrogen from a

[1] Beeck and Ritchie, *Discuss. Faraday Soc.*, 1950, **8**, 159.
[2] Smith and Meriwether, *J. Amer. Chem. Soc.*, 1949, **71**, 413.
[3] Anderson, *Austral. J. Chem.*, 1957, **10**, 409.

cylinder, attached at A, was purified by diffusion through the palladium thimble B. The pressure of hydrogen was controlled by the device H which allowed excess of hydrogen to escape to the rotary pump through a sintered disc, normally covered by mercury but uncovered when the pressure rose to a predetermined value. Hydrocarbons were stored in either of the traps C and protected from contamination by the mercury cut-offs. During each run the appropriate trap C was maintained at a slightly higher temperature than trap D which controlled the partial pressure of hydrocarbon in the stream of hydrogen. The vessel G was packed with gold foil to remove mercury from the gases entering the reaction vessel R. The gold foil was purged periodically by heating it to 250° and passing a stream of hydrogen over it in the reverse direction. The reaction vessel was protected from stopcock grease by cooling the traps E during the preparation of the catalyst, and these traps were also cooled to the same temperature as trap D during each run. U-shaped sample tubes with stopcocks on each limb were attached at S to collect samples of the condensable gases for analysis by gas–liquid chromatography. Provision, not shown in Fig. 1, was made for the evacuation of each sample

FIG. 1. *Plan of the apparatus.*



tube so that there was no danger of air diffusing back into the reaction vessel when tubes were changed during a run. The flow-rate of hydrogen was controlled by the needles-valve V and measured by the calibrated flowmeter F. Pressures in the apparatus were measured by a McLeod guage at J.

B.D.H. " spectroscopically pure " benzene and " laboratory reagent " cyclohexene were dried over sodium wire and dissolved gases were removed by repeated freezing and evacuation. The purity of both substances was checked by gas–liquid chromatography. Each catalyst was prepared from a 9" length of 0·5 mm. " pure " nickel wire (Johnson Matthey) coiled into a spiral which was attached by mild-steel connectors to 1 mm. tungsten leads sealed through the glass of the reaction vessel.

The reaction vessel was baked at 450° for 2 hr. at 10^{-5} to 10^{-6} mm. Hg, and the nickel wire was degassed by passing a current of 4·7 A for the final 30 min. of this period. The films were prepared with the reaction vessel surrounded by an ice-bath and a current of 6·4 A through the nickel spiral. In the early experiments, the catalyst was used without further treatment but in all the subsequent work the film was annealed for 30 min. at 50° in a pressure of a few mm. of hydrogen. The area of films treated in this manner was 890 $cm.^2$/10 mg., as measured by the adsorption of krypton.* *X*-Ray investigation of the films indicated that they consisted of randomly oriented nickel crystallites.

The material collected in the sample tubes was analysed by gas–liquid chromatography

* Unpublished work by E. Crawford.

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through a 6 ft. column of " dinonyl phthalate " supported on " Celite 545 " at 45°, with detection of the compounds by thermal conductivity. Hydrogen was used as carrier gas at a flow-rate of 70 ml./min. and the pressure difference across the column was 45 cm. Hg with the input at atmospheric pressure. Peak areas were used in preference to peak heights for the estimation of the various hydrocarbons, and calibrations were carried out for each substance. Considerable tailing of the peaks occurred when the material was injected into the column directly from the sample tubes. Consequently, the technique was improved by distilling the material into a smaller space which was then heated according to a standard procedure before the hydrogen stream was passed through it in order to sweep the vapours into the column. Silicone high-vacuum grease was used on all stopcocks in the sampling system and the gas–liquid chromatographic apparatus.

Results

Hydrogenation of Benzene.—The standard reaction mixture contained a partial pressure of 1 mm. of benzene and 100 mm. of hydrogen. This large excess of hydrogen was used in order to avoid undesirable side reactions such as the polymerisation of the unsaturated compound on the nickel surface.[3]

Fig. 2. *Plot of the percentage conversion of benzene into cyclohexane against the reciprocal of the space velocity. Inset shows the influence of the pressure of hydrogen on the conversion at 20°.*

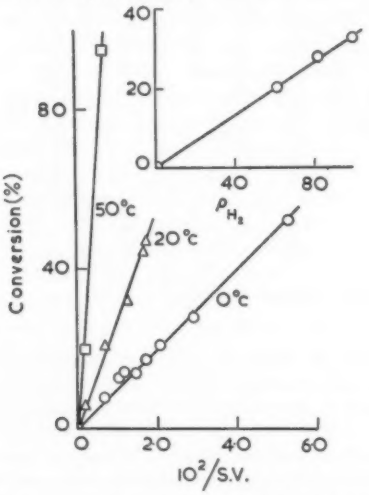
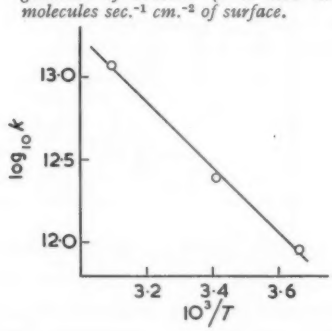


Fig. 3. *Arrhenius plot for the hydrogenation of benzene (k is rate in molecules sec.$^{-1}$ cm.$^{-2}$ of surface.*



Early work with unannealed films revealed the presence of both cyclohexene and cyclohexane as products of hydrogenation of benzene at temperatures between 0° and 50°. Each sample was collected for about 20 min. The proportion of cyclohexene was substantially lower in the second and subsequent samples in each experiment, and as the results were not reproducible no kinetic data were obtained for the conversion of benzene into cyclohexene. This anomalous behaviour was almost eliminated by annealing the films in hydrogen at 50°; there were however still traces of cyclohexene in the first sample and evidence for a slightly greater production of cyclohexane than in the second and subsequent samples, these showing a steady catalytic conversion with no product other than cyclohexane for the duration of each experiment (normally 3—4 hr.). All further work was carried out with annealed films.

Typical results for the reaction at 0°, 20°, and 50° are shown in Fig. 2 as conversion against the reciprocal of the space velocity. This parameter was defined as the total volume (litres measured at S.T.P.) of gas flowing per hour per unit volume (ml.) of catalyst, and was evaluated by assuming that the density of the films was the normal density of nickel. The reciprocal

of the space velocity is a measure of the contact time between the reactants and the catalyst. Any influence of the reaction on the space velocity can be neglected as the reaction mixture contained only 1% of hydrocarbon. The linear plots are consistent with (*a*) a catalytic activity proportional to the volume, and hence the weight, of the nickel films and (*b*) a zero-order dependence of the rate of reaction on the partial pressure of benzene.

A series of experiments at 20° under identical conditions, except for the use of three different partial pressures of hydrogen, are shown in the inset of Fig. 2 and they indicate that the conversion is of first order with respect to hydrogen pressure.

The rate of reaction (k) in molecules sec.$^{-1}$ cm.$^{-2}$ of nickel surface was evaluated from the equation $k = XQ\boldsymbol{N}/(22{,}400 \times 89w)$ where Q is the flow-rate of hydrocarbon in ml. (S.T.P.) sec.$^{-1}$, $\boldsymbol{N}$ is Avogadro's number, X is the fraction of the benzene converted at a partial pressure of hydrogen of 100 mm., and w is the weight of the catalyst in mg. Rates obtained in this manner are shown in Fig. 3, and the Arrhenius plot corresponds to $E = 9{\cdot}0 \pm 0{\cdot}5$ kcal. mole^{-1} and $A = 1{\cdot}5 \times 10^{19}$ molecules sec.$^{-1}$ cm.$^{-2}$ of surface in the equation $k = A \exp(-E/\boldsymbol{R}T)$.

Hydrogenation of Cyclohexene.—The standard reaction mixture contained a partial pressure of 1·26 mm. of cyclohexene and 40 mm. of hydrogen. Results obtained at −22·9° and −34·6° are shown in Fig. 4 and they are similar to those for benzene, given in Fig. 2, except

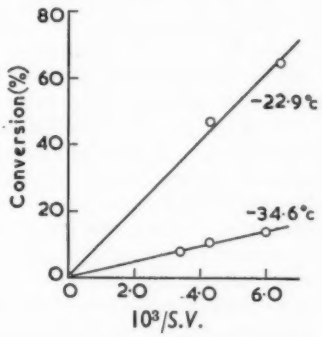


FIG. 4. *Plot of the percentage conversion of cyclohexene into cyclohexane against the reciprocal of the space velocity.*

that the reaction was much more rapid. It was not possible to obtain reliable data for the order of the reaction with respect to the pressure of the hydrogen because the palladium thimble would not deliver sufficient hydrogen to maintain the high flow-rate needed to control the rate of the reaction under higher partial pressures of hydrogen than about 40 mm. The reaction was also so fast that it could not be studied over a sufficiently wide range of temperature to derive an accurate activation energy. The average value of the rates at the two temperatures were 3·1 and 0·7 $\times$ 10^{13} molecules sec.$^{-1}$ cm.$^{-2}$ of surface under the standard pressure of hydrogen of 40 mm., and these correspond to an activation energy of 15 $\pm$ 2 kcal. mole^{-1}. The straight lines in Fig. 4 indicate that the reaction was of zero order with respect to cyclohexene pressure, and no products other than cyclohexane were observed.

DISCUSSION

Our results for the hydrogenation of benzene are in general agreement with those obtained by Beeck and Ritchie.[1] They found the activation energy to be 8·7 kcal. mole^{-1} which is close to our value of 9·0 kcal. mole^{-1}. They report a zero-order dependence on benzene pressure but a 0·44th order with respect to hydrogen pressure, whereas our rate was of first order for the hydrogen-dependence and this seems in better agreement with the results for other hydrogenations.[4] By using the results given by Beeck and Ritchie for a nickel film at 21·5°, it is possible to calculate the rate of the reaction as 2·5 $\times$ 10^{12} molecules sec.$^{-1}$ cm.$^{-2}$ of surface (based on a size of their reaction vessel of 400 ml., an area of 900 cm.^{2}/10 mg. nickel; their pressure-dependence is used to correct from an initial pressure

[4] Smith in "Catalysis," Vol. V (ed. Emmett), Reinhold, New York, 1957, p. 175.

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of hydrogen of 342 mm. to our standard pressure of 100 mm.). Our rate at this temperature is $2{\cdot}9 \times 10^{12}$ in the same units. The agreement is satisfactory considering that our films were sintered at 50° whereas theirs were sintered at 23° and also that they were working with a relatively low ratio of hydrogen to hydrocarbon with the possibility of some poisoning of the film. We conclude from the agreement between the two investigations that we have been successful in avoiding any substantial contamination of the surface during our experiments with the flow system.

It is interesting to compare the rate of hydrogenation of cyclohexene with the rate of exchange of cyclohexane and deuterium on nickel films examined by Anderson and Kemball.[5] They found an activation energy of 10·8 kcal. mole^{-1} and a rate at −34° of $1{\cdot}1 \times 10^{12}$ molecules sec.$^{-1}$ cm.$^{-2}$ of surface, using 1 mm. of hydrocarbon and 19 mm. of deuterium, whereas our rate of hydrogenation with 40 mm. of hydrogen was 7×10^{12} molecules sec.$^{-1}$ cm.$^{-2}$ of surface. The rate-determining step in the exchange is the conversion of adsorbed cyclohexyl radicals into gaseous cyclohexane molecules (this will be the same as the rate of dissociative adsorption of cyclohexane under the conditions prevailing in an exchange reaction). It is possible that the same rate-determining step is involved in the hydrogenation of cyclohexene and that a somewhat greater rate of reaction is obtained because the surface is more extensively covered with adsorbed cyclohexyl radicals in the hydrogenation than in the exchange reaction. It seems clear that the relative strengths of adsorption are cyclohexene > hydrogen > cyclohexane, and this means that the kinetics of the two reactions are quite different. The hydrogenation is of zero order with respect to olefin and probably of first order in hydrogen, whereas the exchange reaction, at any rate on palladium, is of first order with respect to cyclohexane and inversely dependent on the pressure of deuterium.

The rate of hydrogenation of cyclohexene at −34·6°, *i.e.*, 7×10^{12} molecules sec.$^{-1}$ cm.$^{-2}$ of surface, is some 200 times faster than the corresponding rate of $3{\cdot}2 \times 10^{10}$ for the hydrogenation of benzene under a pressure of 40 mm. of hydrogen. Even greater disparity between the two rates occurs at higher temperature because the activation energy for the hydrogenation of cyclohexene exceeds that for the hydrogenation of benzene, *e.g.*, the ratio at 25° is about 3000 ± 1500.

Thermodynamic data [6] indicate that the addition of a hydrogen molecule to benzene to form cyclohexa-1,3-diene is endothermic to the extent of 5·6 kcal. mole^{-1}. The remaining stages in the formation of cyclohexane are strongly exothermic and, consequently, we shall assume that the slow step in the hydrogenation of benzene is the conversion of adsorbed C_6H_6 into adsorbed C_6H_8. The increase of heat content for this step will depend on the relative strengths of adsorption of the two species under the conditions used for the catalytic reaction as well as on the change of heat content given above. Three possible mechanisms will be considered.

Mechanism (1). The reaction takes place between a gaseous molecule of hydrogen and chemisorbed benzene which is assumed to cover the surface. The appropriate expression according to absolute-rate theory is closely analogous to that given by Glasstone, Laidler, and Eyring [7] for the immobile adsorption of a gas on a surface. The rate is given by

$$v_1 = C_{H_2} C_B \frac{kT}{h} \frac{f^*}{F_{H_2} f_B} \exp(-\varepsilon_1/kT) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where v_1 is the rate of reaction in molecules sec.$^{-1}$ cm.$^{-2}$ of surface, C_{H_2} the concentration of hydrogen in the gas phase in molecules cm.$^{-3}$, and C_B the concentration of adsorbed benzene in molecules cm.$^{-2}$ F_{H_2}, f^*, and f_B are the partition functions of hydrogen (at unit

[5] Anderson and Kemball, *Proc. Roy. Soc.*, 1954, *A*, **226**, 472.
[6] Kistiakowsky, Ruhoff, Smith and Vaughan, *J. Amer. Chem. Soc.*, 1936, **58**, 137, 146.
[7] Glasstone, Laidler, and Eyring. "The Theory of Rate Processes," McGraw-Hill, New York, 1941, p. 349

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concentration), the activated complex, and adsorbed benzene respectively, and the other constants have the usual meaning.

Mechanism (2). The slow step is the addition of a chemisorbed hydrogen atom to a chemisorbed C_6H_7 species. The latter are assumed to be in equilibrium with adsorbed benzene molecules which cover almost all the surface and with hydrogen atoms which are weakly adsorbed on a fraction θ_H of the C_s sites available in the spaces between the benzene molecules. The value of θ_H is given by

$$\theta_H = \frac{C_H}{C_s} = C_{H_2}^{\frac{1}{2}} \frac{f_H}{f_s F_{H_2}^{\frac{1}{2}}} \exp(\varepsilon_2/kT) \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where f_s is the partition function of a site and the other terms require no definition. Considering the equilibrium

$$(C_6H_6)_{ads.} + (H)_{ads.} \rightleftharpoons (C_6H_7)_{ads.} + (\text{vacant site})$$

it follows that

$$C_{BH} = \frac{C_B C_H}{C_s} \frac{f_{BH} f_s}{f_B f_H} \exp(\varepsilon_3/kT) \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The rate of reaction is given by

$$v_2 = C_{BH}\theta_H \frac{kT}{h} \frac{f^* f_s}{f_{BH} f_H} \exp(-\varepsilon_4/kT) \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and substitution from (2) and (3) gives

$$v_2 = C_B \theta_H^2 \frac{kT}{h} \frac{f^* f_s^2}{f_B f_H^2} \exp[-(\varepsilon_4 - \varepsilon_3)/kT] \quad . \quad . \quad . \quad . \quad (5)$$

and this expression reduces to (1) with

$$\varepsilon_1 = \varepsilon_4 - \varepsilon_3 - 2\varepsilon_2$$

after further substitution from (2).

Mechanism (3). The rate-determining step is the simultaneous addition of two adsorbed hydrogen atoms to chemisorbed benzene with other conditions as specified for mechanism (2). It is clear that the rate is given by expression (5).

It follows that it is impossible to distinguish by means of absolute-rate theory between these three mechanisms all of which correspond to a reaction which is of zero order with respect to benzene and first order with respect to hydrogen.

Evaluation of equation (1) using the experimental activation energy and assuming that a benzene molecule occupies 40 Å^2 and that the ratio $f^*/f_B = 1$ gives a rate of $2{\cdot}5 \times 10^{13}$ molecules sec.$^{-1}$ cm.$^{-2}$ of surface at 25° and a pressure of 100 mm. of hydrogen. The experimental rate is a factor of 7 lower, *i.e.*, $3{\cdot}5 \times 10^{12}$. This agreement is satisfactory considering the nature of the assumptions that have to be made. Further improvement in the agreement can be obtained if it is assumed that adsorbed benzene has greater freedom, *i.e.*, a higher partition function, than the activated complex. For instance, the adsorbed benzene molecule may have one degree of rotational freedom about the axis perpendicular to the plane of the ring which is lost when they form the activated complex. This would give $f^*/f_B = 1/4{\cdot}4$ and bring the calculated and experimental rates into excellent agreement.

It is premature to attempt to calculate the rate of hydrogenation of cyclohexene until evidence is available about the order of reaction with respect to hydrogen pressure. However, it seems possible that some revision of the ideas about normal rates of hydrogenation may be necessary. The tendency at the present time is to regard the rates of

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hydrogenation of cyclohexene and ethylene as normal and to consider the hydrogenation of benzene as unusually slow. Our calculations suggest that benzene reacts at the expected rate and hence that the catalytic hydrogenation of olefins may be abnormally rapid reactions.

One of us (W. F. M.) was the holder of a Musgrave Studentship. The authors thank Dr. D. Brennan for assistance in the development of the apparatus.

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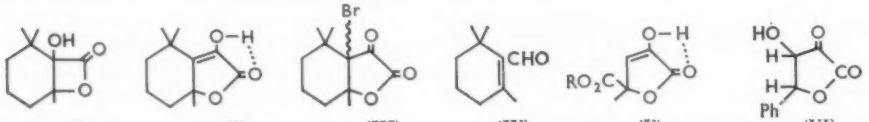
55. *The Constitution of an Oxidation Product of β-Ionone.*

By C. J. W. BROOKS, G. EGLINTON, and D. S. MAGRILL.

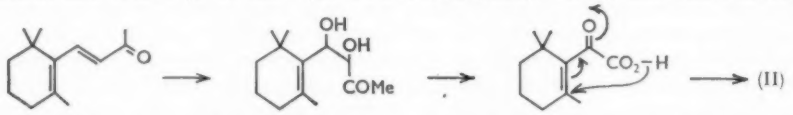
Permanganate oxidation of β-ionone yields the enolic α-keto-lactone (II). Infrared absorption data are discussed.

THE compound, " hydroxyionolactone," m. p. 130°, obtained by Tiemann [1] from β-ionone by permanganate oxidation, was later formulated [2] as a β-lactone (I). Doubts about this structure prompted a re-examination of the oxidation. Under conditions based on those described,[1] a product was isolated resembling Tiemann's lactone in melting point, solubility, acidic character, and reactivity towards bromine. However, Tiemann reported that hydrobromic acid reacted (under unstated conditions) to give a saturated bromolactone, formulated as $C_{10}H_{15}O_2Br$ without physical or analytical data. Our oxidation product was recovered (60%) on addition of water to its solution in 50% hydrobromic–acetic acid. The identity of the two oxidation products is thus not certain, but seems very probable. The results described below indicate that our compound has structure (II), in which the angular methyl group must be axially oriented.



(I) (II) (III) (IV) (V) (VI)

Analyses were in accord with the formula $C_{11}H_{16}O_3$. The presence of an enolic group was shown by a strong ferric reaction. The functional groups were defined by infrared absorption bands (in dilute CCl_4; see Table) at 3507m (intramolecularly bonded OH), *ca.* 3300w (dimer? hydroxyl; absent in very dilute solution), 1760vs (αβ-unsaturated γ-lactone), and 1702m (C=C) cm.$^{-1}$ (no COOH absorption), and by ultraviolet absorption



maxima [238 mμ (ε 11,400) in EtOH; 274 mμ (ε 10,000) in ethanolic 0·003N-NaOH]. These results, in particular the ultraviolet absorption, are typical of an enolised α-keto-lactone,[3] and lead to the expression (II): the formally alternative δ-lactonic structure is excluded by the infrared data. The lactone readily formed an acetate, m. p. 66—67°, and with diazomethane slowly gave what is regarded as an *O*-methyl derivative by analogy [3b,4] and from

[1] Tiemann, *Ber.*, 1898, **31**, 857.
[2] Simonsen, " The Terpenes," Cambridge Univ. Press, 2nd edn., 1947, Vol. I, p. 128; Rodd, " Chemistry of Carbon Compounds," Elsevier, Amsterdam, 1953, Vol. II, p. 503.
[3] (*a*) Djerassi and Rittel, *J. Amer. Chem. Soc.*, 1957, **79**, 3528; (*b*) Schinz and Hinder, *Helv. Chim. Acta*, 1947, **30**, 1349; (*c*) Plattner and Jampolsky, *ibid.*, 1943, **26**, 689.
[4] Stacy, Cleary, and Gortakowski, *J. Org. Chem.*, 1957, **22**, 765.

infrared data. Bromine water was decolorised by the lactone (cf. ref. 3*b*), the product being the β-bromo-α-keto-lactone (III; possibly a mixture of stereoisomers), which showed elevated carbonyl frequencies as found in other non-enolised α-dicarbonyl compounds.[5] Pyrolysis[6] of the lactone (II) gave β-cyclocitral (IV), isolated as its 2,4-dinitrophenylhydrazone which was identical with authentic material.[7] A plausible route for the formation of the lactone (II) would involve a diol intermediate (cf. ref. 8) as in the annexed scheme.

Spectroscopic data were observed for comparison from the compounds (V; R = H, Me). The ultraviolet absorption, and in particular the " alkali shift " due to ionisation of the enol [pK_2 6·95 for the acid (V; R = H)[9]] closely resembled that found for the lactone (II). Infrared data for the ester (V; R = Me) are listed in the Table together with data for related systems. A band near 3510 cm.$^{-1}$ does not necessarily indicate an α-enolic carbonyl system, for saturated α-ketols may have (usually broader) bands in this region (*e.g.*, 3505 cm.$^{-1}$ for a D-homosteroid 17α-hydroxy-17a-ketone[10]). The saturated α-hydroxy-γ-lactone, pantolactone, absorbs at 3565 cm.$^{-1}$. Confusion is unlikely to arise with the monomer hydroxyl band of a carboxylic acid (3535—3515 cm.$^{-1}$) as the typical acid dimer hydroxyl absorption near 3000 cm.$^{-1}$, and the corresponding dimer carbonyl band (approx. 40 cm.$^{-1}$ below the monomer band) both persist to extremely high dilutions.

Hydroxyl and carbonyl stretching frequencies for α-enolic carbonyl compounds.

	ν_{OH}	$\Delta\nu_{\frac{1}{2}}$ [a]	ε_a	ν_{OH} (dimer?)	ν_{CO}	$\Delta\nu_{\frac{1}{2}}$ [a]	ε_a	$\nu_{C=C}$	ε_a
Lactone [a] (II)	3507	26	195	(3350) †	1760	13	(1400)	1702	(120)
Lactone [a] (V; R = Me) ...	3516	30	130	(3348) †	1787 [d]	12	(880)	1697	(130)
Lactone [b] (VI)	(3509)	*	*	*	(1776)	*	*	(1709)	*
Lactone [c] from iresin	3546	*	*	3333	1757	*	*	1681	*
3-Methylcyclopentane-1,2-dione [a]	3505	29	110	—	1723	9	620	1677	590
Maltol [a] (2-hydroxy-3-methyl-4-pyrone).....	3398	65	70	—	1640	11	1510	1679	150

Values in parentheses are approximate. * Not measured. † Band reduced to insignificance by dilution. [a] Present work: CCl_4 solutions. [b] Ref. 11: CH_2Cl_2 solution (cited as μ). The β-hydroxyl group may contribute to the band recorded. [c] Ref. 3*a*: $CHCl_3$ solution. [d] Ester-carbonyl absorption at 1748 cm.$^{-1}$, $\Delta\nu_{\frac{1}{2}}$ 17, ε_a 530.

In the α-hydroxy-γ-pyrone, maltol (see Table), in which an α-enolic carbonyl group forms part of a larger conjugated system, the monomer hydroxyl band is broader and of lower frequency. When examined in the solid or liquid state, α-enolic lactones, like diosphenols, exhibit strong hydroxyl absorption in the range 3300—3400 cm.$^{-1}$ [*e.g.*, lactone (II), 3350 (KBr); α-oxo-β-hydroxy-γ-phenylbutyrolactone[11] (VI), *ca.* 3367 (Nujol); tetrahydrogentiogenins,[12] *ca.* 3300 (KBr) cm.$^{-1}$]; the monomer band is insignificant. The carbonyl band tentatively attributed to a dimeric form of lactone (II) occurs at 1737 cm.$^{-1}$ (KBr) [cf. lactone (VI), *ca.* 1748 cm.$^{-1}$ (Nujol); α-oxo-βγ-diphenylbutyrolactone,[11] *ca.* 1730 cm.$^{-1}$ (Nujol)]. The bands ascribed to double-bond stretching vibrations in lactones (II), (V), and (VI) are at frequencies somewhat above the usual range.

Experimental

Unless otherwise specified, ultraviolet absorption data (determined with a Unicam S.P. 500 spectrophotometer) are for EtOH solutions, and infrared data for CCl_4; apparent extinction coefficients (ε_a) are in l. mole^{-1} cm.$^{-1}$. Infrared measurements were made as described elsewhere[13] with a Unicam S.P. 100 infrared spectrometer equipped with a prism-grating double

[5] Alder, Schäfer, Esser, Krieger, and Reubke, *Annalen*, 1955, **593**, 23.
[6] Schinz and Rossi, *Helv. Chim. Acta*, 1948, **31**, 1953.
[7] Naves and Ardizio, *Bull. Soc. chim. France*, 1954, 330.
[8] Wiberg and Saegebarth, *J. Amer. Chem. Soc.*, 1957, **79**, 2822; Waters, *Quart. Rev.*, 1958, **12**, 277.
[9] Montgomery and Webb, *J. Biol. Chem.*, 1956, **221**, 359.
[10] Wendler, Taub, Dobriner, and Fukushima, *J. Amer. Chem. Soc.*, 1956, **78**, 5027.
[11] Dahn and Hauth, *Helv. Chim. Acta*, 1957, **40**, 2249, 2261.
[12] Korte, *Chem. Ber.*, 1954, **87**, 769.
[13] Brooks, Eglinton, and Morman, *J.*, 1961, 106.

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monochromator. Light petroleum refers to the fraction of b. p. 40—60°. Microanalyses were performed by Mr. J. M. L. Cameron and his associates.

Oxidation of β-Ionone.—The β-ionone used was 98% pure as shown by gas–liquid chromatography and ultraviolet spectrometry. A solution of potassium permanganate (40 g.) in water (600 ml.) was added dropwise, in 2½ hr., to a stirred solution of β-ionone (20 g.) in acetone (220 ml.) and water (60 ml.), at 0—5°. Then sodium acetate (*ca.* 5 g.) was added, and the mixture was treated with sulphur dioxide, saturated with sodium chloride, and extracted with ether (4 × 300 ml.). The combined ether phases were extracted with saturated sodium hydrogen carbonate solution (4 × 100 ml.). Acidification of the alkaline phase and ether-extraction yielded a yellow oil (11 g.), which after several extractions with boiling water gave a waxy solid, m. p. *ca.* 122°: the infrared spectrum (Nujol) indicated the presence of carboxylic acid impurities. Recrystallisation from water followed by sublimation at 70°/0·1 mm. gave the lactone (II), **2,4,5,6,7,7a-*hexahydro*-3-*hydroxy*-4,4,7a-*trimethylbenzofuran*-2-*one***. The m. p. was obscured by extensive sublimation, and was unsharp (129—131°) whether determined on the Kofler block or in a capillary tube (Found: C, 67·4; H, 8·0. $C_{11}H_{16}O_3$ requires C, 67·35; H, 8·2%). The compound gave a red-violet colour with ferric chloride, and failed to give a 2,4-dinitrophenylhydrazone under the usual conditions.

Reactions of the Oxidation Product (II).—(i) The lactone (25 mg.) was kept overnight with pyridine (0·2 ml.) and acetic anhydride (0·15 ml.). The *acetate*, after sublimation and recrystallisation from ether–light petroleum, formed prisms (15 mg.), m. p. 66—67° (Found: C, 65·5; H, 7·15. $C_{13}H_{18}O_4$ requires C, 65·5; H, 7·6%), $\lambda_{max.}$ 216·5 mμ (ε 14,000) (cf. ref. 3*c*), $\nu_{max.}$ 1787vs and 1776vs (lactone and enolic acetate CO), 1677 (conjugated C=C) cm.$^{-1}$.

(ii) The lactone (29 mg.) was kept at 5° for 24 hr. with ethereal diazomethane (3 mol.); one drop of methanol and a further 2 mol. of diazomethane were then added. The solution was worked up after a further 24 hr., yielding the impure methyl ether as an oil which after two short-path distillations at 0·1 mm. amounted to 11 mg. (Found: C, 67·85; H, 8·75. Calc. for $C_{12}H_{18}O_3$: C, 68·55; H, 8·65%), $\lambda_{max.}$ 226 mμ (ε 11,000), $\nu_{max.}$ 1763 (ε_a 1150) (lactone CO), 1660 (ε_a 110) (C=C), 2868 and 2845 (C–H of OMe) cm.$^{-1}$.

(iii) A suspension of the lactone (80 mg.) in water (25 ml.) was shaken while bromine water (2 ml.; 35 mg./ml.) was added during 10 min. The precipitated *bromo-derivative* (III) recrystallised from ether–light petroleum as prisms (65 mg.), m. p. 166—173° (forming a glass: further recrystallisation did not improve the m. p.) (Found: C, 48·2; H, 5·65; Br, 29·25. $C_{11}H_{15}O_3Br$ requires C, 48·0; H, 5·5; Br, 29·05%), apparent $\lambda_{max.}$ (in ether) *ca.* 225 mμ (ε 3000), $\nu_{max.}$ 1810 (ε_a *ca.* 650), 1781 (ε_a *ca.* 290) cm.$^{-1}$ (no OH absorption).

(iv) The lactone (50 mg.) was kept under nitrogen in a tube containing a cold finger, immersed for 10 min. in a bath at 300°. The volatile oil (14 mg.) recovered had $\lambda_{max.}$ 246 mμ: the intensity of absorption was consistent with the presence of 63% of pure β-cyclocitral,[7] which was isolated as the 2,4-dinitrophenylhydrazone and, recrystallised from ether–light petroleum (yield, 6·5 mg.), had m. p. and mixed m. p. 171—172°, $\lambda_{max.}$ (in $CHCl_3$) 386 mμ (ε 26,000). The infrared spectrum (KCl disc) was identical with that of an authentic sample.[7]

α-Enolic Lactones.—γ-Carboxy-α-oxo-γ-valerolactone (V; R = H), isolated from commercial pyruvic acid,[14] had m. p. 115—116°, $\lambda_{max.}$ 237 mμ (ε 6200) (in 0·003N-NaOH–EtOH), 270 mμ (ε ~8000) (in 0·003N-HCl–EtOH), 234 mμ (ε 6400), isosbestic point, 249 mμ (ε 4000), $\nu_{max.}$ (Nujol) 3300—2400 (CO_2H), 1770 (γ-lactone), *ca.* 1713 (CO_2H), 1670 and 1655 (C=C?) cm.$^{-1}$, and was insoluble in carbon tetrachloride. The *methyl ester* (V; R = Me), prepared with the calculated amount of diazomethane at −30° and purified by short-path distillation, formed viscous gum (Found: C, 44·75; H, 5·25. $C_7H_8O_5,H_2O$ requires C, 44·2; H, 5·3%), $\lambda_{max.}$ 234·5 mμ (ε *ca.* 6000) (in 0·003N-NaOH–EtOH), 270 mμ (ε *ca.* 6000), isosbestic point, 249 mμ (ε *ca.* 3000).

We thank Professor D. H. R. Barton, F.R.S., and Professor R. A. Raphael for their interest, and Mrs. F. Lawrie for infrared measurements. We are indebted to Dr. Y.-R. Naves (Givaudan et Cie) for a sample of β-cyclocitral 2,4-dinitrophenylhydrazone, and to Mr. R. Bell of Roche Products Ltd., Dalry, for a gift of purified β-ionone.

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Chemistry Department, The University, Glasgow, W.2.

[*Received, July 11th,* 1960.]

[14] Hughes and Watson, *J.*, 1929, 1945.

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56. *The Conductance of Solutions in which the Solvent Molecule is "Large." Part VII.*[1] *Solutions in Triaryl Phosphites.*

By C. M. French and R. C. B. Tomlinson.

The conductances of four quaternary ammonium toluene-*p*-sulphonates in four triaryl phosphites at 15°, 25°, 45°, and 65°, over a concentration range $6{\cdot}0 \times 10^{-6}$ to $7{\cdot}9 \times 10^{-3}$N are reported, together with the characteristic P–O–C(aryl) bond-stretching frequencies in the infrared spectra of the phosphites. Simple theories of ion-pair and triple-ion formation account for the general pattern of the conductance data. Ion-atmosphere effects are negligible. Ion-dipole and ion-pair–solvent interactions depending on both the dipole moment and the geometry of the solvent molecules, are suggested to account for the extremely low conductances in these systems, and for certain apparently anomalous variations in ion-pair dissociation constants.

Recent work on the conductance of systems in which the solvent molecules and solute ions do not differ markedly in size, and both are large compared with the molecules of a more usual solvent which may be treated conventionally as a homogeneous continuum, has included the use of dialkyl phthalates,[2] dialkyl alkylphosphonates,[1] and trialkyl and triaryl phosphates [3,4] as solvents. For reasons already enumerated [5] it proved impossible generally to compare the conductance relations of solutions in trialkyl phosphites and phosphates, but the possible influence of solvent structure on conductometric behaviour was thought to be of sufficient interest for measurements to be made in triaryl phosphites as well as in tritolyl phosphite, previously studied.[3] However, in view of the readiness with which many phosphorous acid esters are oxidised, it was deemed advisable to use, as solutes, quaternary ammonium salts other than picrates which are commonly employed in these investigations, and as the toluene-*p*-sulphonates could readily be prepared these were chosen for the present work.

Experimental

Conductances were measured as previously described [1] by means of the Jones and Josephs type bridge for the most highly conducting solutions, and by the Schering bridge for the more poorly conducting ones. Cells of both conventional parallel-plate design, and with 3 concentric platinum electrodes were employed. Cell constants K were determined by Deitz and Fuoss's method,[6] from the air capacitance of the cells measured by the Schering bridge, and checked by the capacitance of the cells filled with standard liquid (benzene or carbon tetrachloride). K for the 3-electrode cell $= 6{\cdot}658 \times 10^{-4}$; constants of the various parallel-plate cells employed were of the order of 10^{-3}.

Dielectric constants were determined at 10^6 c./sec. as previously described,[1] benzene ($\varepsilon^{25} = 2{\cdot}274$) being used as standard. The refractive index of each solution of the phosphite in benzene was also measured at 25° by means of an Abbé refractometer, and the dipole moments of the phosphorous acid ester molecules were calculated by using the relation given by Smith [7] for benzene as solvent at 25°, *viz.*, $_{\mu}P_2 = 0{\cdot}18811M_2\alpha - 0{\cdot}19064M_2\nu$, where M_2 is the molecular weight of the phosphorous acid ester, and α and ν are the limiting values at infinite dilution of $\delta\varepsilon/\delta w_2$ and $\delta n^2/\delta w_2$ respectively, w_2 being the weight fraction of the ester in the solution. From this we have

$$\mu = (_{\mu}P_2 \cdot 9\boldsymbol{k}T/4\pi\boldsymbol{N})^{\frac{1}{2}}$$

[1] Parts V and VI, French and Hart, *J.*, 1960, 1671, 1679.
[2] French and Singer, *J.*, 1956, 1424, 2428.
[3] French and Muggleton, *J.*, 1957, 5064.
[4] French, Hart, and Muggleton, *J.*, 1959, 358.
[5] French and Hart, *J.*, 1960, 3161.
[6] Dietz and Fuoss, *J. Amer. Chem. Soc.*, 1938, **60**, 2394.
[7] Smith, "Electric Dipole Moments," Butterworths, London, 1955, p. 61.

The tetra-alkylammonium toluene-*p*-sulphonates * used as solutes were all prepared by one or both of the two alternative procedures: (1) Refluxing the appropriate tertiary amine in benzene with the corresponding ester of toluene-*p*-sulphonic acid, itself prepared by the interaction at −5° to −10° of dry pyridine solutions of recrystallised toluene-*p*-sulphonyl chloride and the appropriate alcohol.[8] The time of refluxing depended on the ester used (2 hr. for ethyl, 20 hr. for n-propyl, and 100 hr. for n-butyl ester). Cooling resulted in the deposition of tetraethyl- and tetra-n-propyl-ammonium toluene-*p*-sulphonates, but the tetra-n-butyl-ammonium salt had to be extracted with water which was then removed by vacuum distillation, and desiccation (P_2O_5). (2) Neutralising toluene-*p*-sulphonic acid with the appropriate quaternary ammonium hydroxide in aqueous or aqueous-ethanolic solution. In the case of the tetra-n-propylammonium salt the solvent was then removed by vacuum distillation and desiccation (P_2O_5). With the three lower homologues, water was removed by refluxing with benzene in a Dean–Stark apparatus.

Purification of the toluene-*p*-sulphonates was effected by recrystallisation from aqueous solutions refluxed with benzene (Me_4NTos), from ethyl acetate and cooling in carbon dioxide–acetone (Et_4NTos), from benzene (Et_4NTos and Pr^n_4NTos), and from ethyl acetate (Bu^n_4NTos).

TABLE 1. *Solvent properties.**

	Triphenyl phosphite				*Tri*-m-*tolyl phosphite*			
B. p.	134°/0·14 mm. (lit.[9] 360°/760 mm., 200°/5 mm.)				174°/0·17 mm. (lit. 240—243°/10 mm.,[10] 248—250°/12 mm.[12])			
n_D^{20}	1·5900 (lit.[13] n_D^{25} 1·58801) [13]				1·5758			
μ^{25}	1·71				1·89			
Temp.	15°	25°	45°	65°	15°	25°	45°	65°
d_4^t	1·191	1·182	1·164	1·145	1·134	1·126	1·110	1·094
η	25·18	14·26	6·950	4·060	37·55	21·17	9·132	5·075
ε	3·79	3·75	3·67	3·57	3·67	3·61	3·53	3·49
$10^{10}\kappa$	4·597	8·961	24·85	45·72	2·083	5·706	20·50	49·70
	Tri-p-*tolyl phosphite*				*Tri*-p-*ethylphenyl phosphite*			
B. p.	180°/0·18 mm. (lit. 250—255°/10 mm.,[10] 285°/11 mm.[11])				180°/0·18 mm.			
n_D^{20}	1·5759				1·5650			
μ^{25}	2·05				2·08			
Temp.	15°	25°	45°	65°	15°	25°	45°	65°
d_4^t	1·134	1·127	1·111	1·095	1·104	1·096	1·082	1·066
η	35·23	20·17	8·794	5·017	30·23	18·80	9·047	5·274
ε	3·88	3·83	3·74	3·64	3·74	3·70	3·61	3·51
$10^{10}\kappa$	0·6275	1·602	6·840	16·78	0·2845	1·096	5·079	9·245

* μ = dipole moment (D); η = viscosity (cp.); ε = dielectric constant; κ = specific conductivity (ohm^{-1} cm.$^{-1}$).

The physical data and analyses of the *toluene*-p-*sulphonates* are as follows: Tetramethyl-ammonium salt, m. p. 241—242°, d_4^{20} 1·21 (Found: C, 53·5; H, 7·3; N, 5·8; S, 13·25. $C_{11}H_{19}O_3NS$ requires C, 53·85; H, 7·8; N, 5·7; S, 13·1%), tetraethylammonium salt, m. p. 112°, d_4^{20} 1·15 (Found: C, 58·7; H, 9·0; N, 4·9; S, 10·8. $C_{15}H_{27}O_3NS$ requires C, 59·8; H, 9·0; N, 4·65; S, 10·6%); tetra-n-propylammonium salt, m. p. 106—107°, d_4^{20} 1·12 (Found: C, 63·75; H, 9·5; N, 3·9; S, 8·6. $C_{19}H_{35}O_3NS$ requires C, 63·8; H, 9·9; N, 3·9; S, 9·0%); tetra-n-butylammonium salt, m. p. 100—101°, d_4^{20} 1·09 (Found: C, 61·4; H, 9·8; N, 3·7; S, 7·6. $C_{23}H_{43}O_3NS$ requires C, 66·8; H, 10·5; N, 3·4; S, 7·75%).

The three larger solvents, tri-*p*-tolyl, tri-*m*-tolyl, and tri-*p*-ethyl-phenyl phosphite were prepared by mixing the appropriate phenol (after redistillation) with phosphorus trichloride in stoicheiometric quantities below 20°, raising the temperature to 160° during 6 hr., and distilling off the resulting phosphite. Subsequent purification of these esters and of triphenyl

* This anion will be denoted in formulæ as " Tos."

[8] Tipson, *J. Org. Chem.*, 1944, **9**, 235.
[9] Beilstein, " Handbuch der Organischen Chemie," 4th Edn., Springer, Berlin, 1922, XI, p. 103.
[10] Michaels and Kühne, *Ber.*, 1898, **31**, 1048.
[11] Strecker and Grossman, *Ber.*, 1916, **49**, 63.
[12] Broeker, *J. prakt. Chem.*, 1928, **118**, 287.
[13] Lewis and Smyth, *J. Amer. Chem. Soc.*, 1940, **62**, 1529.

TABLE 2. *Equivalent conductivity* Λ (ohm^{-1} cm.^{2}) *at concentration* c (*equiv./l.*).

TABLE 2. *Equivalent conductivity* Λ (*ohm*$^{-1}$ *cm.*^{2}) *at concentration* c (*equiv./l.*).

1. *Conductance in triphenyl phosphite of:*

(*a*) Tetramethylammonium toluene-*p*-sulphonate

15°				25°				45°				65°			
10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$
23·83	0·4452	6·965	0·4681	23·65	0·8661	6·912	0·8926	23·29	2·696	6·807	2·420	22·91	5·818	6·696	5·075
14·71	0·4218	3·317	0·9135	14·60	0·8144	3·292	1·590	14·37	2·395	3·242	4·130	14·14	4·994	3·189	8·078
13·60	0·4193	1·870	1·517	13·50	0·8007	1·856	2·670	13·29	2·326	1·828	6·132	13·07	4·895	1·798	10·92
10·21	0·4098			10·13	0·7989			9·974	2·234			9·811	4·791		

(*b*) Tetraethylammonium toluene-*p*-sulphonate

67·46	4·809	11·67	4·255	66·95	8·993	11·58	8·294	65·93	24·39	11·41	23·81	64·86	52·41	11·22	55·25
46·65	4·191	9·774	4·630	46·29	7·894	9·744	8·843	45·59	21·89	9·552	25·82	44·85	47·80	9·397	59·25
32·09	3·780	7·912	5·029	31·84	7·230	7·852	9·533	31·36	20·37	7·732	28·19	30·85	45·45	7·607	64·51
22·36	3·626	7·051	5·286	22·19	6·895	6·998	10·10	21·85	19·54	6·891	29·43	21·50	45·10	6·779	67·71
20·26	3·558	4·933	6·311	20·11	6·778	4·896	11·72	19·80	19·68	4·821	34·39	19·48	44·72	4·743	80·65
14·94	4·035	4·892	6·333	14·82	7·713	4·855	11·84	14·60	22·25	4·781	34·60	14·36	50·60	4·703	82·25
		3·193	7·579			3·169	13·94			3·121	41·49			3·070	95·02

(*c*) Tetra-n-propylammonium toluene-*p*-sulphonate

76·69	6·980	10·00	4·027	76·11	12·79	9·928	7·733	74·94	33·15	9·776	21·75	73·73	68·62	9·617	50·22
46·64	5·281	6·589	4·609	46·29	9·754	6·539	8·489	45·58	26·06	6·439	23·71	44·85	55·09	6·335	54·65
30·24	4·292	6·336	4·719	30·01	8·261	6·288	8·542	29·55	22·78	6·192	23·84	29·08	49·17	6·092	55·02
25·95	4·243	4·347	5·374	25·75	8·012	4·314	9·277	25·36	22·38	4·248	27·12	24·95	48·78	4·179	64·20
19·30	3·911	3·957	5·722	19·15	7·546	3·927	9·745	18·86	21·77	3·868	27·90	18·55	48·15	3·805	65·20
15·78	3·947	2·961	6·930	15·66	7·522	2·938	11·40	15·42	21·17	2·893	31·50	15·17	47·75	2·846	74·31
10·54	4·013	2·323	7·667	10·46	7·697	2·305	12·49	10·30	21·66	2·270	35·32	10·13	49·17	2·233	83·03
		1·255	9·211			1·245	16·33			1·226	43·00			1·207	99·59

(*d*) Tetra-n-butylammonium toluene-*p*-sulphonate

58·48	6·943	7·379	4·365	58·02	12·76	7·323	8·423	57·15	33·65	7·212	24·93	56·22	70·35	7·095	57·22
33·62	5·223	4·422	4·878	33·37	9·730	4·389	9·148	32·86	27·08	4·322	27·65	32·33	58·34	4·052	64·65
18·58	4·316	3·101	5·434	18·44	8·400	3·077	10·56	18·16	24·05	3·030	30·46	17·87	52·85	2·981	74·04
12·87	4·226	2·317	6·055	12·77	8·168	2·300	11·89	12·57	23·85	2·265	35·23	12·37	53·81	2·228	82·72
12·44	4·225	2·149	6·640	12·35	8·138	2·133	12·98	12·16	24·10	2·100	35·79	11·96	53·39	2·066	83·74
9·408	4·225	0·9110	9·391	9·336	8·206	0·9041	17·31	9·194	24·68	0·8903	46·00	9·045	56·66	0·8759	103·0

2. *Conductance in tri-*m*-tolyl phosphite of:*

(*a*) Tetraethylammonium toluene-*p*-sulphonate

2·450	0·9442	1·170	1·505	2·433	1·988	1·162	3·144	2·398	7·414	1·156	11·68	2·364	21·35	1·129	34·45
2·365	0·9809	0·8620	1·789	2·349	2·028	0·8559	3·800	2·315	7·439	0·8438	13·68	2·282	21·66	0·8316	40·87
1·310	1·400	0·6771	2·144	1·301	2·828	0·6723	4·651	1·282	10·52	0·6627	15·33	1·264	31·12	0·6532	48·98

(*b*) Tetra-n-propylammonium toluene-*p*-sulphonate

15·11	1·757	1·575	1·269	15·00	3·572	1·564	2·822	14·79	10·27	1·542	10·64	14·57	24·78	1·469	31·01
7·936	1·390	1·523	1·270	7·880	2·774	1·512	2·884	7·768	9·001	1·491	11·00	7·656	21·03	1·012	41·86
6·262	1·301	1·049	1·291	6·218	2·677	1·042	3·083	6·129	8·805	1·027	12·32	6·041	21·36	0·6552	69·50
2·710	1·231			2·691	2·685			2·653	9·413	0·6648	19·55	2·615	25·58	0·3639	94·60
										0·3692	25·66	1·520	31·57		

(*c*) Tetra-n-butylammonium toluene-*p*-sulphonate

10·04	1·400	0·8650	1·640	9·968	2·953	1·418	2·939	9·826	9·431	1·398	10·67	9·685	22·16	1·378	32·34
6·195	1·218	0·7514	1·859	6·151	2·685	0·8589	4·291	6·063	8·756	0·8467	16·49	5·976	20·52	0·8345	52·73
4·528	1·184			4·496	2·620	0·7461	4·519	4·432	8·595	0·7355	18·98	4·368	22·01	0·7249	59·59
2·977	1·181			2·956	2·574			2·914	8·937	0·5128	20·38	2·872	24·93	0·5054	70·35
2·703	1·192			2·684	2·607			2·646	9·184	0·5101	22·69	2·608	26·03	0·5028	77·31
1·428	1·327			1·532	2·873			1·510	10·50	0·3358	28·09	1·489	31·57	0·3310	101·1

TABLE 2. (*Continued.*)

3. *Conductance in tri-*p*-tolyl phosphite of:*

(*a*) Tetramethylammonium toluene-*p*-sulphonate

15°				25°				45°				65°			
10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$	10^4c	$10^4\Lambda$
1·029	2·155	0·1468	8·046	1·023	4·241	0·1459	15·14	1·008	13·16	0·1438	42·88	3·567	11·73	0·9940	30·63
0·4843	3·371	0·06207	13·64	0·4814	6·796	0·06169	25·43	0·4745	22·12	0·06081	68·52	2·607	12·61	0·4677	53·10
												1·560	20·82	0·1417	97·95
														0·05993	167·5

(*b*) Tetraethylammonium toluene-*p*-sulphonate

15·70	1·586	2·520	2·256	15·61	3·527	2·504	4·722	15·39	10·71	2·469	16·33	15·16	24·06	2·433	45·69
12·19	1·579	2·360	2·400	12·12	3·351	2·346	4·999	11·95	9·762	2·313	17·23	11·78	23·35	2·279	47·99
8·254	1·571	1·359	3·193	8·203	3·261	1·351	6·678	8·086	10·63	1·332	24·37	7·970	26·32	1·312	72·05
7·175	1·605	0·7953	4·999	7·130	3·354	0·7904	10·29	7·029	11·61	0·7792	38·55	6·928	26·16	0·7680	111·7
4·576	1·734	0·5537	6·904	4·547	3·587	0·5503	13·10	4·483	12·58	0·5425	52·43	4·418	32·31	0·5346	152·5
4·377	1·774	0·3748	10·14	4·350	3·743	0·3725	19·33	4·289	13·05	0·3672	74·00	4·227	33·17	0·3619	215·3

(*c*) Tetra-n-propylammonium toluene-*p*-sulphonate

18·29	1·996	2·788	2·061	18·18	4·181	2·770	4·563	17·92	11·86	2·731	16·87	17·66	27·92	2·692	43·04
14·74	1·767	1·531	2·769	14·65	3·728	1·521	6·166	14·44	10·93	1·500	22·34	14·23	26·24	1·478	58·13
10·58	1·710	1·059	3·584	10·51	3·596	1·052	7·786	10·36	11·22	1·037	30·18	10·21	27·59	1·022	70·61
6·973	1·667	0·7847	4·649	6·930	3·660	0·7798	10·42	6·831	11·70	0·7687	39·58	6·733	29·86	0·7577	103·3
5·866	1·742	0·4712	6·220	5·830	3·702	0·4683	13·05	5·747	11·82	0·4617	44·92	5·664	31·44	0·4550	115·7
2·810	2·056	0·4029	6·781	2·792	4·551	0·4004	14·25	2·753	16·75	0·3947	49·66	2·713	42·75	0·3890	123·0

(*d*) Tetra-n-butylammonium toluene-*p*-sulphonate

14·33	2·922	1·266	5·385	14·25	5·722	1·258	11·27	14·04	17·17	1·240	35·89	13·84	39·70	1·223	78·54
9·511	2·750	0·9477	6·545	9·453	5·296	0·9419	13·88	9·319	16·31	0·9285	42·77	9·184	37·80	0·9152	98·30
7·941	2·768	0·4701	10·11	7·892	5·400	0·4672	19·84	7·780	16·34	0·4606	58·53	7·668	38·77	0·4539	137·4
6·472	2·801	0·4601	10·19	6·432	5·602	0·4573	20·07	6·341	17·20	0·4508	59·57	6·249	40·96	0·4443	139·9
3·245	3·394	0·1447	18·66	3·225	6·680	0·1438	38·16	3·179	20·04	0·1418	114·8	3·134	48·76	0·1397	272·7
2·666	3·578			2·649	7·258			2·612	23·31			2·574	53·29		

4. *Conductance in tri-*p*-ethylphenyl phosphite of:*

(*a*) Tetraethylammonium toluene-*p*-sulphonate

2·088	1·753	0·7741	3·838	2·074	3·430	0·7688	7·306	2·046	9·799	0·7587	21·74	2·016	24·32	0·7475	51·63
1·412	2·566	0·4517	4·933	1·403	5·009	0·4487	9·203	1·384	14·21	0·4427	29·44	1·364	33·56	0·4362	77·18
0·9268	3·479	0·3128	5·892	0·9205	6·653	0·3107	10·69	0·9083	19·05	0·3066	33·83	0·8950	46·11	0·3021	94·30

(*b*) Tetra-n-propylammonium toluene-*p*-sulphonate

5·382	1·268	1·667	1·691	5·343	2·401	1·654	3·257	5·275	7·007	1·633	9·551	5·197	15·69	1·609	23·12
5·105	1·275	1·202	1·840	5·068	2·409	1·193	4·238	5·003	7·192	1·178	11·41	4·929	15·70	1·161	27·02
2·880	1·415	1·156	1·864	2·859	2·649	1·148	4·330	2·823	7·913	1·133	11·82	2·781	18·79	1·117	27·26
2·841	1·423	0·5890	2·744	2·820	2·682	0·5847	6·255	2·784	7·998	0·5773	16·34	2·743	18·80	0·5687	37·41
1·723	1·688	0·2462	4·950	1·711	3·167	0·2440	9·401	1·689	9·289	0·2413	27·69	1·664	22·49	0·2377	61·93

(*c*) Tetra-n-butylammonium toluene-*p*-sulphonate

5·357	1·813	1·844	2·310	5·318	3·275	1·831	3·934	5·250	9·815	1·808	11·63	5·173	22·07	1·781	28·39
3·475	1·817	1·307	2·658	3·450	3·384	1·298	4·571	3·406	9·913	1·281	13·37	3·355	24·44	1·262	32·37
3·147	1·819	0·9619	3·150	3·124	3·445	0·9549	5·205	3·084	10·05	0·9427	15·44	3·039	25·09	0·9288	35·73
1·992	2·231	0·4716	4·157	1·978	3·829	0·4681	6·854	1·952	11·44	0·4622	20·08	1·924	27·53	0·4553	63·35

phosphite (purchased from Albright & Wilson Ltd.) was by distillation at reduced pressure in oxygen-free nitrogen. Physical data for the solvents are given in Table 1.

Results.—The variation in equivalent conductance with concentration at four temperatures for the systems studied is shown in Table 2.

Discussion

The Λ–$c^{\frac{1}{2}}$ plots for all systems exhibited the expected marked curvature typical of weak electrolytes, and in many cases minima were observed in the more concentrated solutions. According to Walden,[14] $\varepsilon^3/c_{\text{min.}} = \text{constant}$ (approximately 3×10^4), and the data given in Table 3 show this empirical rule to be closely followed for solutions in triphenyl phosphite, but that increasingly great divergences are obtained with tri-*p*-tolyl

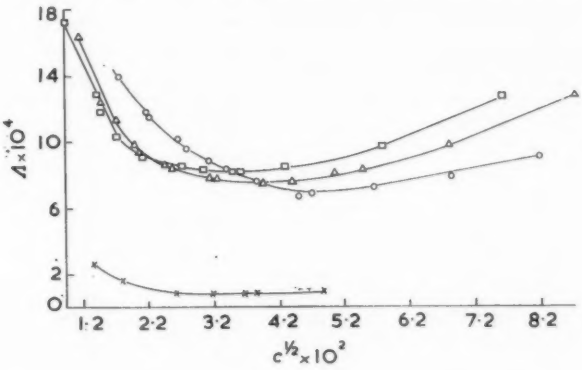

Fig. 1. *Solutions in triphenyl phosphite at* 25°.

× Me_4NTos. ○ Et_4NTos.
△ Pr_4NTos. □ Bu_4NTos.

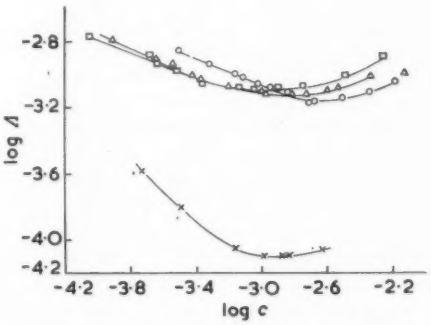

Fig. 2. *Solutions in triphenyl phosphite at* 25°.
(Key as in Fig. 1.)

and tri-*m*-tolyl phosphites. The low solubility of the solutes in tri-*p*-ethylphenyl phosphite prevented observation of the conductance minima in this solvent. It will also be noticed that in all cases, the value of $\varepsilon^3/c_{\text{min.}}$ decreases steadily with increase in temperature. The Λ–$c^{\frac{1}{2}}$ curves also demonstrate that the conductance of tetraethylammonium toluene-*p*-sulphonate is exceptionally low at all temperatures compared with that of the other toluene-*p*-sulphonates. A typical set of curves is shown in Fig. 1.

log Λ–log c plots tended towards the ideal limiting case of straight line with slope $-\frac{1}{2}$ in the most dilute regions in most systems, but deviations from linearity occurred at concentrations considerably less than that of the minima in the curves (examples are given in Fig. 2), indicating appreciable triple-ion formation in this region. The existence of triple ions was further confirmed by the linearity of the $\Lambda c^{\frac{1}{2}}$–c plots down to concentrations of the order of 2—5×10^{-4}N.

[14] Walden, *Z. phys. Chem.*, 1930, **147**, *A*, 1.

The Ostwald dilution function in the form given by Kraus and Bray [15] was employed to investigate further the equilibria in these systems. The plots of $1/\Lambda$ against $c\Lambda$ showed two distinct regions joined by a line of steep gradient. The lower end of the discontinuity occurs at concentrations of the order of $0{\cdot}5$—$1{\cdot}0 \times 10^{-4}$N, which is only a little greater than the value of $1{\cdot}2$—$1{\cdot}8 \times 10^{-5}$N for the critical concentration in these systems, predicted from the Fuoss relation $c_{\text{crit.}} \simeq 3 \times 10^{-7} \times \varepsilon^3$. At concentrations up to the lower discontinuity, therefore, the free ion–ion-pair equilibrium appears to govern the magnitude of the conductance. The upper limit of the discontinuity occurs at concentrations of

TABLE 3. *Conductance minima, ion-pair dissociation constants, Bjerrum "* a *" parameters, and mean values of* ΔH^0.

Solute	Mean ΔH°		15°	25°	45°	65°
1. *Solutions in triphenyl phosphite*						
		$10^{-4}\varepsilon^3/c_{\text{min.}}$	5·32	4·84	4·54	4·45
Me_4NTos	5·63	10^8K	0·177	0·267	0·505	0·747
		"*a*" (Å)	6·97	6·94	6·83	6·73
		$10^{-4}\varepsilon^3/c_{\text{min.}}$	2·57	2·44	2·82	1·98
Et_4NTos	6·53	10^8K	27·79	38·64	78·54	145·1
		"*a*" (Å)	9·89	9·94	10·08	10·28
		$10^{-4}\varepsilon^3/c_{\text{min.}}$	3·40	3·14	2·94	2·71
Pr_4NTos	6·07	10^8K	25·54	37·27	70·39	122·7
		"*a*" (Å)	9·83	10·10	9·83	10·11
		$10^{-4}\varepsilon^3/c_{\text{min.}}$	4·20	4·07	3·42	2·71
Bu_4NTos	7·10	10^8K	23·92	33·36	76·23	149·6
		"*a*" (Å)	9·76	9·80	10·03	10·32
2. *Solutions in tri-*m*-tolyl phosphite*						
		$10^{-4}\varepsilon^3/c_{\text{min.}}$	13·00	10·68	8·69	6·29
Pr_4NTos	8·49	10^8K	1·54	2·68	6·17	14·8
		"*a*" (Å)	8·21	8·35	8·44	8·49
		$10^{-4}\varepsilon^3/c_{\text{min.}}$	13·70	13·03	9·10	6·80
Bu_4NTos	8·94	10^8K	1·35	2·08	5·75	13·7
		"*a*" (Å)	8·14	8·20	8·38	8·45
3. *Solutions in tri-*p*-tolyl phosphite*						
		$10^{-4}\varepsilon^3/c_{\text{min.}}$	—	—	—	—
Me_4NTos	—	10^8K	—	—	—	4·97
		"*a*" (Å)	—	—	—	7·42
		$10^{-4}\varepsilon^3/c_{\text{min.}}$	6·08	5·66	4·40	3·83
Et_4NTos	6·88	10^8K	5·67	8·12	17·0	33·2
		"*a*" (Å)	8·40	8·48	8·55	8·62
		$10^{-4}\varepsilon^3/c_{\text{min.}}$	6·71	6·24	4·40	3·72
Pr_4NTos	7·92	10^8K	5·74	9·10	21·1	44·5
		"*a*" (Å)	8·47	8·55	8·62	8·85
		$10^{-4}\varepsilon^3/c_{\text{min.}}$	6·08	5·49	4·53	3·94
Bu_4NTos	6·28	10^8K	17·4	22·6	45·8	84·98
		"*a*" (Å)	9·13	9·19	9·32	9·45
4. *Solutions in tri-*p*-ethylphenyl phosphite*						
Pr_4NTos	7·03	10^8K	2·24	3·27	6·61	14·6
		"*a*" (Å)	8·23	8·22	8·25	8·34
Bu_4NTos	6·83	10^8K	3·36	5·33	10·2	20·5
		"*a*" (Å)	8·48	8·51	8·54	8·68

$1{\cdot}2$ — $5{\cdot}5 \times 10^{-4}$N, where deviations from linearity of the $\Lambda c^{\frac{1}{2}}$–c graphs also appear, and above these concentrations triple-ion formation is thus well established. In the intermediate region of concentration between the discontinuity limits, there is a transition between the relative contributions of ion-pair and triple-ion equilibria, and, as expected, this region moves to lower concentrations as the dielectric constant of the solvent decreases.

An accurate estimate of Λ_0 could not be obtained for the present systems since reliable extrapolations of conductance data to infinite dilution were not possible. This is due to the low specific conductance of solutions of dilutions at which binary equilibrium is dominant, and the consequent relatively high solvent conductance, ranging from 5 to 10%

[15] Kraus and Bray, *J. Amer. Chem. Soc.*, 1913, **35**, 1315.

of that of the solution. It was, nevertheless, thought desirable to obtain some estimate of the order of magnitude of Λ_0 in these systems, and approximate values were therefore obtained as follows. Data from successive runs on each system fell on the same smooth curve when Λ was plotted against $c^{\frac{1}{2}}$, and interpolated points were taken in each case from the region of this graph more dilute than that of the lower discontinuity of the Ostwald plot of the original data. These points were used for plots of the Ostwald function. By applying the method of least squares to the interpolated points Λ_0 was calculated from the intercepts of these plots. (Ostwald plots are justified in the present solvents since the low dielectric constant results in ion-pair formation at high dilution, but in only very slight ion-atmosphere effects.) In these systems, where the relative size of the solvent conductance renders impracticable this treatment of the data in the dilute region, use was made of an earlier observation [2] that in homologous series of solvents with "large" molecules $\Lambda_0\eta$ decreases almost linearly with decrease in dielectric constant. Values of the Walden product obtained by graphical estimation of Λ_0 in tri-*p*-tolyl phosphite at 65° were therefore plotted against the dielectric constants of the solvents, and the data for the remaining systems calculated from the interpolated points. The resulting values of Λ_0 are shown in Table 4.

TABLE 4. *Limiting equivalent conductance* ($10^2\Lambda_0$).

Solvent	15°	25°	45°	65°	Solvent	15°	25°	45°	65°
Triphenyl phosphite	1·6	2·5	5·2	8·9	Tri-*p*-tolyl phosphite	1·0	1·8	4·1	7·2
Tri-*m*-tolyl phosphite	0·96	1·7	3·9	7·1	Tri-*p*-ethylphenyl phosphite	1·2	1·9	4·0	6·8

Examination of the data revealed, first, that the values of Λ_0 and hence of $\Lambda_0\eta$ for the three larger solutes in a given solvent and at a given temperature were identical within the limits of the method of determination. There are therefore no very great differences in solvation of the ions of the different solutes by the molecules of a given solvent. Although few data could be obtained, this is further shown by the virtual absence of temperature effect on the Walden product, the values obtained at 45° from limiting equivalent conductances in tri-*p*-tolyl phosphite being almost identical with those at 65°.

The second well-defined feature is the consistently higher values of Λ_0 at all temperatures in triphenyl phosphite than in the other three solvents. The close similarity of the values in the isomeric tritolyl phosphites is also noteworthy, that in the tri-*p*-tolyl ester being always a little higher than that in the *meta*-isomer. The cross-over in Λ_0 values in tri-*p*-ethylphenyl phosphite and its immediately preceding homologue as temperature increases from 15° to 65°, is associated with the lower temperature coefficient of viscosity of the former solvent. The temperature coefficient of conductance also decreases with increase in molecular weight of these solvents. Finally, of special interest is the extremely low order of magnitude of Λ_0 in all systems, implying a considerable retardation of movement of the ions in these solvents, occasioned perhaps by extensive even if loose solvation, or by steric hindrance due to particular configurations of the solvent molecules.

From these values of Λ_0 approximate values of the ion-pair dissociation constants K were obtained by using the relation for triple-ion formation (again with neglect of ion-atmosphere effects), *viz.*,

$$\Lambda = \Lambda_0 K^{\frac{1}{2}}/c^{\frac{1}{2}} + \lambda_0(Kc)^{\frac{1}{2}}/K_3$$

where λ_0 is the sum of the limiting conductances of the two kinds of triple ion, and K_3 the triple-ion dissociation constant. By differentiation of this equation, imposing the conditions for a minimun (or maximum), and substitution of the resulting value of K_3 back into the original equation, we have

$$K = (c\Lambda^2)_{\text{min.}}/4(\Lambda_0)^2$$

In the three smaller solvents, K was estimated from the positions of the conductance minima by using this equation. This reduced the possible error due to the relative size

of the solvent corrections which, at the conductance minima, were less than 1% of the solution conductances. The absence of well-defined minima in the concentration range studied in tri-*p*-ethylphenyl phosphite which was limited by the low solubility of the solutes in this ester, rendered this method impossible here, and K was accordingly deduced from the intercept $\Lambda_0 K^{\frac{1}{2}}$ of the plot of $\Lambda c^{\frac{1}{2}}$ against c. The values af K are given in Table 3.

Noteworthy features in the dissociation constants are, first, the very low values, which are 10—100 times less even than in several other " large " solvent molecule systems,[1-3] and secondly, that, as expected,[6] in solvents of low dielectric constant, K increases significantly with increase in temperature. This again is in contrast to the variable behaviour found in other systems in this series of investigations.[1-3] Certain well-marked tendencies are also discernible with change in cation size, but their significance is perhaps more easily discussed in terms of the ion-pair radius derived from K by means of the Bjerrum equation [17] and shown in Table 3. One apparent anomaly in K values should be noted. According to Bjerrum's equation K should decrease with decrease in dielectric constant, and this is observed for solutions in both the tritolyl and tri-*p*-ethylphenyl phosphites. However, if the structurally similar solvents, triphenyl, tri-*p*-tolyl, and tri-*p*-ethylphenyl phosphites are considered, the markedly larger K values in the first of these esters is unexpected in view of its smaller dielectric constant compared with that of the tolyl ester. The explanation for this phenomenon may nevertheless be related to ion-solvent interaction as discussed below.

A survey of the " a " values shows that, with the exception of tetramethylammonium toluene-*p*-sulphonate in triphenyl phosphite, there is a steady increase in ion-pair radius with increasing temperature, a phenomenon which is paralleled in other large solvent molecule systems.[1,3] In tri-*p*-tolyl and tri-*p*-ethylphenyl phosphites the slight increase in " a " in passing up the homologous series of toluene-*p*-sulphonates might be expected from the slight increase in cation size, and presents no anomaly. The virtual absence of change in " a " in the other two solvents if the tetramethylammonium salt is neglected (the variation in triphenyl phosphite being within the limits of accuracy of estimation in these systems) is perhaps a little surprising, but may be due to the insensitivity of the method of estimation in solvents of very low dielectric constant. Nevertheless, the markedly low " a " value for tetramethylammonium toluene-*p*-sulphonate compared with that of the higher homologues is interesting and suggests the possibility of an abrupt decrease in solvation of this salt.

Various of the characteristic features of the systems now discussed may be explained in terms of ion-solvent association. Since forces between dipoles are less than between ions and dipoles, the existence may be postulated in these systems of each ion surrounded by a close solvent molecule sheath of oriented dipoles. Beyond this first sheath the dipoles rapidly assume randon distribution, and the medium in this region may then be classed as a uniform dielectric. The conductance will thus be due to the movement of the ion-dipole complex under the influence of the applied field. Whether the complex moves as a whole or whether the ion alone moves to a neighbouring site by displacement of an adjacent solvent molecule which is of comparable size to itself, and this is followed by an immediate and consequent reorientation of solvent dipoles, the mobility of the ions will be reduced by the solvation sheath in a way not predicted by the macroscopic viscosity of the solvent. The measured conductance will thereby be greatly reduced, as is observed. Furthermore, this screening of each ion by the bulky solvent molecules is likely to be extremely effective so that, as suggested by Denison and Ramsay,[18] only ions which are in contact can be said to constitute ion-pairs. It is therefore interesting to observe that interionic distances calculated from models of the quaternary ammonium toluene-*p*-sulphonates (Me_4NTos, 7·5; Et_4NTos, 8·4; Pr_4NTos, 9·5; Bu_4NTos, 10·2 Å) do not differ

[16] Kraus, *J. Phys. Chem.*, 1956, **60**, 129.
[17] Bjerrum, *Kgl. danske Videnskab. Selskab*, 1926, **7**, No. 9, 18.
[18] Denison and Ramsay, *J. Amer. Chem. Soc.*, 1955, **77**, 2615.

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widely from the Bjerrum "*a*" parameter shown in Table 3. Finally, efficient screening of this nature would tend to minimise ion-atmosphere effects, and explain the apparent applicability to these systems of equations in which the effect is neglected.

In view of this influence of screening, the dipole moments of the solvent molecules can be expected to be one of the important factors governing the relative magnitudes of conductances in these systems. If tri-*m*-tolyl phosphite, whose structure differs from that of the other phosphites is excluded, the dissociation constants for the salts in the other three structurally similar solvents are in the reverse order of the dipole moments of the solvent molecules, but are not simply related to the solvent dielectric constants (Table 1). However, since the latter also influence conductance, and it is difficult to separate the effect of each factor quantitatively, the overall result is likely to be complex in any given system. The determining part played by the dipole moment in the present systems is revealed owing to the very small variation between the dielectric constants of the solvents.

If the free ions alone were solvated, K should follow the dipole moments of the solvent molecules, and the reverse order observed here suggests that the solvated ion pairs are more stable structures than the solvated free ions in these systems. This is borne out also by the thermodynamic data; ΔG^0 (the free energy of dissociation) was calculated from the equation $\Delta G^0 = -RT \ln K$, and plotted against the absolute temperature. Values of ΔH^0 obtained from the intercept of this graph are shown in Table 3 ($\Delta G^0 = \Delta H^0 - T\Delta S^0$), calculations showing that the 3% uncertainty in K, resulting from the method of estimation noted earlier, had a negligible effect on the ΔH^0 values. The use of $\ln K$–$1/T$ plots for determining ΔH^0 gives essentially the same ΔH^0 values, within the limits of graphical methods of estimation. It was shown by Stern and Martell [19] that when ΔH^0 is positive, as in all the present systems, solvated ion-pairs represent a more stable arrangement than solvated ions. Finally, an unexpectedly large variation in ΔS^0 from solvent to solvent was observed in these systems, although, as shown by Gurney,[20] none is expected when the temperature coefficient of the dielectric constant is the same, as is nearly true for the three structurally similar solvents here. This may be taken as further evidence of the failure of the simple macroscopic dielectric constant to account for the behaviour of this type of system.

Infrared spectra [21] and a study of atomic models suggest that there is a tendency for aryl phosphites to adopt a planar configuration with the lone pair of electrons on the phosphorus atom becoming progressively less shielded by the benzene rings as planarity increases. Data now presented (Table 5) for the O–C and P–O stretching frequencies in

TABLE 5. P–O–C(*aryl*) *bond-stretching frequencies.*

Solvent	Absorption peaks (cm.$^{-1}$)		Solvent	Absorption peaks (cm.$^{-1}$)	
Triphenyl phosphite	1195	1025	Tri-*p*-tolyl phosphite	1199	1019
Tri-*m*-tolyl phosphite	1232	1007	Tri-*p*-ethylphenyl phosphite	1200	1018
Tri-*o*-tolyl phosphite	1224	1045			

the present series of phosphorous acid esters demonstrate an increasing strain in the molecules as the substituents are placed nearer the P–O–C linkages, apparently caused by the mutual repulsion of the aryl groups, thus increasing the tendency to planarity. Models also indicate a restriction of free rotation of the aromatic groups even in triphenyl phosphite, *ortho*- and *meta*-substituents possibly increasing steric hindrance to rotation. This conclusion was substantiated by theoretical calculations by Lewis and Smyth,[13] who also pointed out that the P–O and C–O moments are screened by the phenyl groups. Thus, in addition to the factors already discussed, note must be taken of the effect on conductance and related quantities of the varying geometry of the solvent molecules, especially where

[19] Stern and Martell, *J. Amer. Chem. Soc.*, 1955, **77**, 1983.
[20] Gurney, "Ionic Processes in Solutions," McGraw-Hill, New York, 1953, p. 13.
[21] Bellamy and Beecher, *J.*, 1952, 475.

these are " large." Tri-*m*-tolyl phosphite has a lower dipole moment than that of tri-*p*-tolyl phosphite, and solutes in it might, by the arguments just adduced, be expected to have higher dissociation constants, but the reverse is actually observed. It is suggested that the introduction of *meta*-substituents has caused the mean position of the rings in the solvent molecules to become more planar than in the *ortho*-isomer. The P–O and C–O moments are then less efficiently screened in the *meta*-isomer, the effective ion–dipole and ion-pair–dipole interaction increased, and the K value for the ion-pair of the solute decreased below that expected from the measured dipole moment.

The anomalously low conductance of the tetramethylammonium compared with the other toluene-*p*-sulphonates could be associated with a closer approach of these quaternary ammonium ions to the localised dipoles of the solvent molecules. Models indicate that with triphenyl phosphite in a pyramidal form the tetramethylammonium ion can be completely surrounded by the aryl groups, and the centre of positive charge of the ion lies within 3·5 Å of the P–O and C–O bonds. The extent to which this occurs with the consequent reduction in ion mobility will clearly depend, in part at least, on the degree to which the aryl groups of the particular solvent molecule have achieved a planar configuration, and this in turn must affect the closeness of approach of the ions of the other solutes also. Thus movement of the ions will be retarded and conductance decreased by ion-dipole interaction, which depends both on the magnitude of the dipole moment and on the geometry of the ions and solvent molecules. This retarding effect cannot be fully described by the macroscopic viscosity of the solvent.

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57. *Paper-chromatographic Investigation of the Transglycosylation of N-Arylhexosylamines and Arylamines.*

By R. BOGNÁR, P. NÁNÁSI, and M. PUSKÁS.

Rate of transglycosylation of *N*-arylglycosylamines with other amines has been studied by means of paper chromatography. The relative rates of formation of a new *N*-arylglycosylamine (*a*) by transglycosylation and (*b*) from its components, as well as the hydrolysis of the corresponding glycosylamine, confirmed that the former reaction is a true transglycosylation.

WE report here experiments which in our opinion prove unambiguously that exchange of arylamino-groups between an *N*-arylglycosylamine and a different arylamine is a true transglycosylation (cf. ref. 1); hydrolysis and subsequent reglycosylation are of secondary importance, even in the presence of water.

Our technique consisted of measuring (*a*) the composition of transglycosylation mixtures after various reaction times, using dilute homogeneous solutions, (*b*) the rate of formation of the new glycosylamine from its components, and (*c*) the rate of hydrolysis of the original *N*-arylglycosylamine. Thus, rates of transglycosylation, hydrolysis, and subsequent reglycosylation could be compared.

A method of quantitative paper chromatography was developed for determining *N*-arylglycosylamines and free sugars in the presence of each other, with an accuracy greater than 5%.

[1] Bognár and Nánási, *J.*, 1955, 189; *Acta Chim. Acad. Sci. Hung.*, 1957, **12**, 115; Bognár, Nánási, and Nemes-Nánási, *J.*, 1955, 193.

FIG. 1a. FIG. 1b.

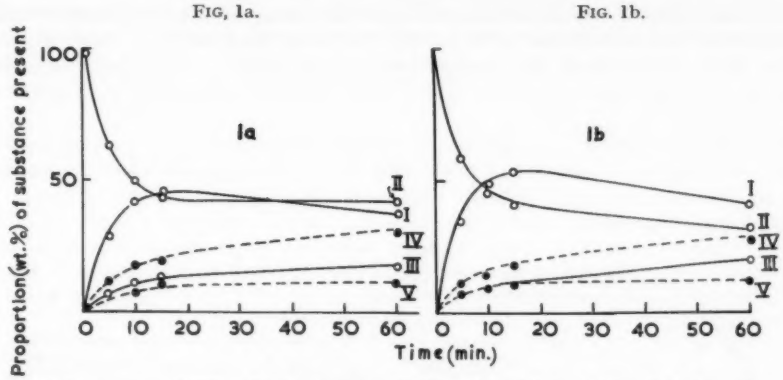

FIG. 1. (a) *In presence of* HCl. (b) *In presence of* HCl *and pyridine. Rates of* (I) *formation of* N-p-*sulphamoylphenyl*-D-*glucosylamine,* (II) *removal of* N-p-*tolyl*-D-*glucosylamine, and* (III) *liberation of* D-*glucose during transglucosylation between* N-p-*tolyl*-D-*glucosylamine and* p-*toluidine.* (IV) *Rate of hydrolysis of* N-p-*tolyl*-D-*glucosylamine.* (V) *Rate of formation of* N-p-*sulphamoylphenyl*-D-*glucosylamine from sulphanilamide and* D-*glucose.*

FIG. 2a, b. FIG. 4a, b.

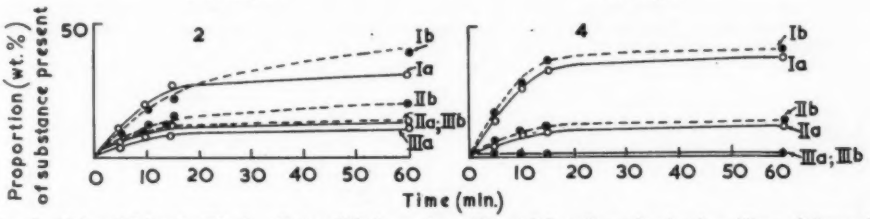

FIG. 2. (a) *and* (b) *as in Fig.* 1. *Rates of* (I) *formation of* N-p-*tolyl*-D-*glucosylamine from* N-p-*sulphamoylphenyl*-D-*glucosylamine and* p-*toluidine,* (II) *hydrolysis of* N-p-*sulphamoylphenyl*-D-*glucosylamine, and* (III) *formation of* N-p-*tolyl*-D-*glucosylamine from* p-*toluidine and* D-*glucose.*

FIG. 4. (a) *and* (b) *as in Fig.* 1. *Rates of* (I) *formation of* N-p-*nitrophenyl*-D-*glucosylamine during transglycosylation between* N-p-*sulphamoylphenyl*-D-*glucosylamine and* p-*nitroaniline,* (II) *as curve* (II) *in* Fig. 2, *and* (III) *formation of* N-p-*nitrophenyl*-D-*glucosylamine from* p-*nitroaniline and* D-*glucose.*

FIG. 3a. FIG. 3b.

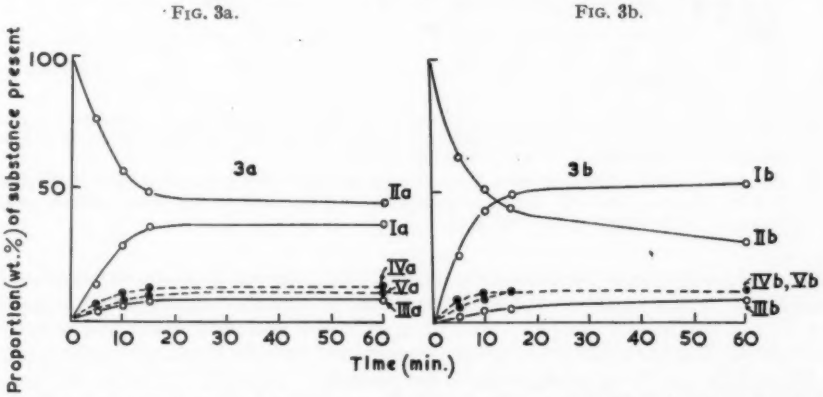

FIG. 3. (a) *and* (b) *as in Fig.* 1. *Rates of* (I) *formation of* N-p-*sulphamoylphenyl*-D-*glucosylamine,* (II) *removal of* N-p-*nitrophenyl*-D-*glucosylamine, and* (III) *liberation of* D-*glucose during transglucosylation between* N-p-*nitrophenyl*-D-*glucosylamine and sulphanilamide.* (IV) *Rate of hydrolysis of* N-p-*nitrophenyl*-D-*glucosylamine.* (V) *As curve* (V) *in Fig.* 1.

In contrast with the preparative experiments, the composition of the reaction medium was chosen to avoid precipitation of either the reagents or the products. Aqueous ethanol 88% was used as the solvent, and hydrochloric acid as catalyst. In parallel experiments a small amount of pyridine was also added, since it was advantageous in transglycosylations.

The results are shown in the Figures. It is apparent that the rate of transglycosylation is, without exception, in all cases considerably higher than that of either hydrolysis or

FIG. 5a, b. FIG. 6a, b.

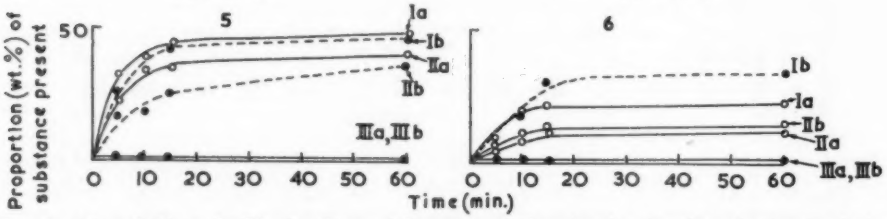

FIG. 5. (a) *and* (b) *as in Fig.* 1. *Rates of formation of* N-p-*nitrophenyl*-D-*glucosylamine* (I) *during transglucosylation between* N-p-*bromophenyl*-D-*glucosylamine and* p-*nitroaniline aud* (III) *from* p-*nitroaniline and* D-*glucose.* (II) *Rate of hydrolysis of* N-p-*bromophenyl*-D-*glucosylamine.*

FIG. 6. (a) *and* (b) *as in Fig.* 1. *Rates of formation of* N-p-*bromophenyl*-D-*glucosylamine* (I) *during transglucosylation between* N-p-*nitrophenyl*-D-*glucosylamine and* p-*bromoaniline and* (III) *from* p-*bromoaniline and* D-*glucose.* (II) *As curve* (IV) *of* Fig. 3.

FIG. 7. FIG. 8.

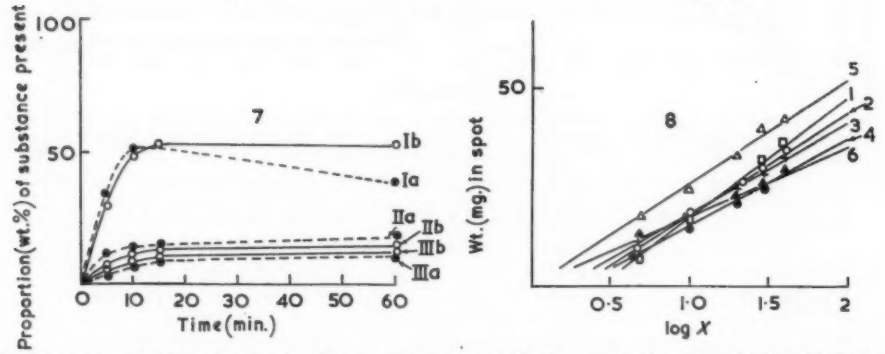

FIG. 7. (a) *and* (b) *as in* Fig. 1. *Rates of formation of* N-p-*bromophenyl*-D-*glucosylamine* (I) *during transglucosylation between* N-p-*sulphamoylphenyl*-D-*glucosylamine and* p-*bromoaniline and* (III) *from* p-*bromoaniline and* D-*glucose.* (II) *As curve* (II) *of* Fig. 2.

FIG. 8. *Calibration curves, for quantitative paper chromatography, of* (1) N-p-*nitrophenyl-*, (2) N-p-*tolyl-*, (3) N-p-*bromophenyl-*, *and* (4) N-p-*sulphamoylphenyl*-D-*glucosylamine,* (5) p-*nitroaniline, and* (6) D-*glucose.* X = *Wt.* (*mg.*) *of material applied.*

formation of *N*-arylglycosylamines, even in the dilute, aqueous solutions employed. The rate of the formation of the new *N*-arylglycosylamine from its components is, in general, lower than the rate of hydrolysis even when only the necessary sugar and amine are present as starting materials, in the proper proportions, from the beginning of the reaction. The Figures also prove the reversibility of the transglycosylation [2] because in each related pair of diagrams (*e.g.*, Figs. 1 and 2) the starting compounds of one are the products of the other.

[2] Cf. Inoue and Onodera, *J. Agric. Chem. Soc. Japan*, 1953, **27**, 5; *Chem. Abs.*, 1955, **49**, 871.

Experimental.—Composition and sampling of the reaction mixture. A solution 0·04M with respect to each of *N*-aryl-D-glucosylamine, D-glucose, and amine was prepared in ethyl alcohol containing 12% of water. In series (*a*) hydrochloric acid (0·016 mol.), or in series (*b*) hydrochloric acid (0·016 mol.) and pyridine (0·025 mol.), were added. The mixture was kept at 40°, and samples (0·1 ml. each) were withdrawn after 5, 10, 15, and 60 min. Reaction was arrested by adding 10% ammonia solution (0·025 ml.) to the samples. Experiments with pure materials showed that under identical conditions no further conversion or hydrolysis of the materials occurred during chromatography.

Analysis by paper chromatography. A portion (0·005 ml.) of the sample was transferred to Schleicher-Schüll No. 2043A paper, and run in butan-1-ol–pyridine–water (6 : 4 : 3). The method of descending chromatography was applied without conditioning of the paper. 10% Aqueous ammonia (5 ml.) was placed in the chamber, and this inhibited further reaction in any direction during chromatography. The running length was 38 cm. in all cases, which required 24 hr. at 20—21°. The area of the spots depended solely on the quantity of the material. The chromatogram papers were allowed to dry at room temperature, sprayed with aniline hydrogen phthalate solution, and dried for 10 min. at 125°. Glycosylamines and free sugars may be detected in this way. The positions of the coloured spots were marked under ultraviolet light.

Quantitative evaluation was by means of calibration curves, prepared by measuring the area of the spots obtained when 5, 10, 20, 30, and 40 μg. of pure *N*-arylglycosylamine and sugar were submitted to chromatography as above. The weight of material in each spot (in mg.), plotted against the logarithm of the quantity of material applied, invariably gave a straight line. Pure materials and components of reaction mixtures of known composition have thus been determined with an error less than 5% (see Fig. 8).

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58. *Preparation of Isomeric* N-*Arylglycosylamines.*

By P. NÁNÁSI and R. BOGNÁR.

A method has been developed for separation of lævo- and dextro-rotatory isomers of *N*-arylglycosylamines after catalytic deacetylation of the anomers or anomeric mixtures of *N*-arylglycosylamine tetra-acetates. Structural problems, of these isomeric probably anomeric forms, are discussed.

CRYSTALLINE isomeric *N*-arylglycosylamines with different melting points and optical rotations have been isolated,[1-3] but their structures have not been precisely determined.

In our opinion, the two isomeric *N*-*p*-tolyl-D-glucosylamines are anomeric, as indicated by their optical activities and mutarotations, and Ellis and Honeyman [4] describe them as *N*-*p*-tolyl-α- and -β-D-glucosylamines, m. p. 135—136°, 117—118°, $[\alpha]_D$ +208·9° ⟶ −44·6°, −100° ⟶ −46° (in MeOH), respectively.

We have prepared isomeric *N*-arylglycosylamines, in all probability anomers, by a novel method, namely hydrolysis of the acetates. In a previous paper [5] we described the separation of isomeric *N*-arylglycosylamine tetra-acetates by various methods, it being assumed that they were α- and β-anomers, and this was supported by our investigations

[1] Berger and Lee, *J. Org. Chem.*, 1946, **11**, 75, 84; Howard, Kenner, Lythgoe, and Todd, *J.*, 1946, 855; Butler, Laland, Overend, and Stacey, *J.*, 1950, 1433; Weygand, Perkow, and Kuhner, *Chem. Ber.*, 1951, **84**, 594; Kuhn and Ströbele, *Ber.*, 1937, **70**, 773; Irvine and Gilmour, *J.*, 1907, 1429; 1909, 1545.
[2] Ellis and Honeyman, *J.*, 1952, 1490.
[3] Rosen, Woods, and Pigman, *J. Org. Chem.*, 1957, **22**, 1727.
[4] Ellis and Honeyman, *Adv. Carbohydrate Chem.*, 1955, **10**, 95.
[5] Bognár and Nánási, *J.*, 1955, 185.

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of their mutarotation.[6] The acetates were hydrolysed at room temperature in concentrated anhydrous methanol solutions, in the presence of 0·1—0·2 mol. of sodium methoxide.[7] The deacetylated products either crystallised directly or were precipitated by ether–light petroleum. The free glycosylamines do not mutarotate in dry methanol alone or in the presence of sodium methoxide, or do so only relatively slowly; so it may be assumed that neither anomerisation nor change in the number of atoms forming the ring occurs to any great extent under the above conditions, so that the pure anomeric acetates afford the pure *N*-arylglucosylamines. Experimentally the products from pure anomeric acetates appeared to be homogeneous. When mixtures of anomeric acetates were hydrolysed, the first fractions precipitated were almost pure α- or β-anomer, depending on the relative solubilities; the other anomer was later isolated from the mother-liquors. From mixed anomeric *N*-*p*-nitrophenyl-D-glucosylamine tetra-acetates and from *N*-*p*-bromophenyl-D-glucosylamine tetra-acetates almost pure, highly lævorotatory β-anomers were first obtained, but a mixture *N*-*p*-tolyl-D-glucosylamine tetra-acetates (80% of the α-anomer) gave first the dextrorotatory α-anomer.[2,3] This α-anomer had a higher dextrorotation than was recorded in the literature; however, when the α-anomer prepared by Pigman's method [3] was extracted with cold anhydrous methanol, the insoluble crystalline residue was identical with the α-anomer obtained by direct saponification.

The *N*-arylglycosylamine isomers obtained by deacetylation are stable in methanolic solution, but in the presence of acids mutarotate in a few minutes to equilibrium values of negative rotation. Exceptions are the *N*-*p*-tolyl-D-glucosylamine isomers which (similarly to the *N*-phenyl-D-glucosylamine isomers [1-3]) mutarotate also in absolute methanol, although very slowly (equilibration requires a few days). This agrees with our earlier observations [6] of a connection between the basicity of the arylamine and the tendency of the *N*-arylglycosylamine to mutarotate.

Treatment of the active glucosylamines at room temperature with acetic anhydride in pyridine gave active tetra-acetates. Dextrorotatory *N*-*p*-bromophenyl-, *N*-*p*-nitrophenyl-, or *N*-*p*-tolyl-D-glucosylamine gave dextrorotatory tetra-acetates; the other isomers gave lævorotatory tetra-acetates. Crystallising the acetylated dextrorotatory *N*-*p*-nitrophenyl-D-glucosylamine gave an α-tetra-acetate stereochemically more homogeneous than that obtained by repeated recrystallisation of the isomeric acetate mixture (cf. ref. 5). During the reacetylation anomerisation occurs only to a small extent, which seems to depend on the basicity of the arylamine. Thus, the α- or β-isomer of *N*-*p*-tolyl-D-glucosylamine gave mixed tetra-acetates, though the α-isomer predominated (about 83% for the α- and 65% for the β-form [5]).

We have assumed that the *N*-arylglycosylamine pairs are anomers because of the mild conditions that have been used in the preparations and conversions. The values of initial specific rotations and of those obtained after mutarotation are in agreement with this.

Experimental

N-p-*Tolyl*-α-D-*glucosylamine*.—(*a*) Mixed *N*-*p*-tolyl-D-glucosylamine tetra-acetates (2 g.; containing about 80% of α-anomer; $[\alpha]_D$ +165° in pyridine) were left in anhydrous methanol (5 ml.) containing N-methanolic sodium methoxide (0·5 ml.) at room temperature for 10 min. The crystals (0·34 g., 27·5%) which separated after the solution had been kept at 0° for an hour were filtered off. They had m. p. 124°, $[\alpha]_D^{22}$ +160° (*c* 0·5 in pyridine).

The mother-liquor was left for a day in a refrigerator. The crystalline precipitate (0·44 g., 36%) had m. p. 140° (decomp.), $[\alpha]_D^{22}$ +194° (*c* 0·5 in pyridine), + 226° (*c* 0·5 in MeOH) (Found: C, 57·65; H, 6·8; N, 5·1. Calc. for $C_{13}H_{19}NO_5$: C, 58·0; H, 7·1; N, 5·2%). A mixed m. p. determination with a product prepared by Pigman's method showed no depression. *N*-*p*-Tolyl-α-D-glucosylamine had been prepared [2,3] with m. p. 135—136°, 133—134°, $[\alpha]_D$ +209° ⟶

[6] Bognár and Nánási, *Magyar Kém. Folyóirat*, 1958, **64**, 66
[7] Cf. Zemplén, *Ber.*, 1926, **59**, 1254.

$-45°$ (in MeOH), $[\alpha]_D$ $+206·4° \longrightarrow -44·9°$. When ether (40 ml.) was added to the mother-liquor after removal of the second crop there separated an additional amorphous material (0·4 g.), $[\alpha]_D$ $-25·2°$ (*c* 0·5 in pyridine).

(*b*) The product, m. p. 134°, $[\alpha]_D$ $+192°$ (*c* 1·0 in pyridine), obtained by Pigman's method was mixed at room temperature with a twenty-fold quantity of anhydrous methanol. The insoluble residue had m. p. 139°, $[\alpha]_D^{22}$ $+225°$ (*c* 0·5 in MeOH), $+194°$ (*c* 0·5 in pyridine).

N-p-*Tolyl*-β-D-*glucosylamine*.—The pure β-tetra-acetate (0·5 g.; $[\alpha]_D$ $-76°$ in pyridine) was deacetylated with anhydrous methanol (1·25 ml.) and N-sodium methoxide (0·1 ml.), as in (*a*) above. No precipitate separated after the solution had been left at 0° for a day. Addition of ether (10 ml.) resulted in instantaneous crystallisation. The product [0·21 g.; m. p. 112° (decomp.)], when recrystallised from anhydrous methanol, had m. p. 117—120°, $[\alpha]_D^{22}$ $-86·8°$ (*c* 0·5 in pyridine), $-101°$ (*c* 0·5 in anhydrous MeOH) (Found: N, 5·0%).

α- and β-Anomers of *N-p*-tolyl-D-glucosylamines mutarotate also in anhydrous methanol. In 110 hr. the α- and the β-anomer attain $[\alpha]_D$ $-40°$ and about $-60°$, respectively.

In the presence of a small amount of hydrochloric acid a transient negative rotation is observed, then both anomers very quickly attain $[\alpha]_D$ $+35°$. It was shown in our previous experiments [6] that this is the result of hydrolysis.

The literature [5,2] records for *N-p*-tolyl-β-D-glucosylamine m. p. 112—113°, 113°, 117—118°, $[\alpha]_D^{24}$ $-101·2° \longrightarrow -45·8°$ (in MeOH), $[\alpha]_D^{18}$ $-101° \longrightarrow -46°$.

N-p-*Tolyl*-α-D-*glucosylamine Tetra-acetate*.—*N-p*-Tolyl-α-D-glucosylamine, $[\alpha]_D$ $+194°$ (in pyridine), was acetylated with acetic anhydride in the presence of pyridine. The crude product (90%), m. p. 115—120°, $[\alpha]_D^{22}$ $+168°$ (*c* 0·5 in pyridine), $+187°$ (*c* 0·5 in MeOH), was recrystallised from methanol to give about 40% of the pure α-acetate, m. p. 143°, $[\alpha]_D^{22}$ $+223°$ (in MeOH) (Found: N, 3·3. Calc. for $C_{21}H_{27}NO_9$: N, 3·2%); in the presence of hydrochloric acid, mutarotation gave $[\alpha]_D$ $+30·2°$ in about 5 min. {lit.,[5,6] $[\alpha]_D$ $+228·3° \longrightarrow +27·8°$ (in MeOH)}.

N-p-*Bromophenyl*-α-D-*glucosylamine*.—*N-p*-Bromophenyl-D-glucosylamine tetra-acetate (2·0 g.; containing about 58% of the α-anomer), $[\alpha]_D$ $+70°$ (in pyridine), was deacetylated in methanol as above. After a day at 0°, the crystals were collected {0·24 g.; m. p. 127—133° (decomp.), $[\alpha]_D^{21}$ $-107°$ (*c* 0·5 in pyridine)}. Ether (40 ml.) and light petroleum (60 ml.) were added to the mother-liquor, and the precipitate was extracted with cold methanol. The insoluble crystals (0·18 g., 13·7%) softened at 150° and melted at 154° (decomp.) and had $[\alpha]_D^{22}$ $+167°$ (*c* 0·5 in pyridine), $+198°$ (*c* 0·5 in MeOH). These were dissolved in methanol (3 ml.)–ether (9 ml.), and light petroleum (9 ml.) was added. The crystals (0·1 g.) obtained after storage at 0° had m. p. 163—164° (decomp.), $[\alpha]_D^{22}$ $+237°$ (*c* 0·5 in MeOH), $+207°$ (*c* 0·5 in pyridine) (Found: N, 4·1. Calc. for $C_{12}H_{16}BrNO_5$: N, 4·2%).

The α- and β-anomer of *N-p*-bromophenyl-D-glucosylamine show barely detectable mutarotation in methanol even in 48 hr. In the presence of hydrochloric acid, both anomers show $[\alpha]_D$ $-22°$ within a few minutes. In 48 hr., $[\alpha]_D$ changed in the positive direction because of hydrolysis.

N-p-*Bromophenyl*-β-D-*glucosylamine*.—Pure β-*N-p*-bromophenyl-D-glucosylamine tetra-acetate (0·35 g.), $[\alpha]_D$ $-65°$ (in pyridine), was deacetylated as described above. The directly precipitated crystals (0·2 g., 86%) had m. p. 150°, $[\alpha]_D^{22}$ $-105°$ (*c* 0·5 in MeOH), $-92·3°$ (*c* 0·5 in pyridine). Recrystallisation of the crude product from four parts of methanol yielded the pure product in a good yield, with m. p. 153°, $[\alpha]_D^{22}$ $-110°$ (*c* 0·5 in MeOH) (Found: N, 4·1%).

N-p-*Bromophenyl*-α-D-*glucosylamine Tetra-acetate*.—Almost pure *N-p*-bromophenyl-α-D-glucosylamine, $[\alpha]_D$ $+192°$ (in MeOH), with acetic anhydride in pyridine gave a product containing mostly the α-tetra-acetate (83%), m. p. 150°, $[\alpha]_D^{22}$ $+159°$ (*c* 0·5 in pyridine), $+154°$ (*c* 0·5 in MeOH), changing in hydrochloric acid to $+35°$ in 5 min. The material was dissolved in ether, and recrystallised by addition of light petroleum. Three recrystallisations gave material of m. p. 149°, $[\alpha]_D^{23}$ $+203°$ (*c* 0·5 in MeOH), which is higher than the recorded value,[5] $+147·0°$ (in MeOH) (Found: N, 2·7%).

N-p-*Bromophenyl*-β-D-*glucosylamine Tetra-acetate*.—*N-p*-Bromophenyl-β-D-glucosylamine, $[\alpha]_D$ $-97°$ (in pyridine), with acetic anhydride in pyridine gave a product (91%), m. p. 156°, $[\alpha]_D$ $-37·5° \longrightarrow +31·8°$ (*c* 1·0 in MeOH–HCl), which, crystallised twice from 90% alcohol, gave pure β-tetra-acetate,[5] m. p. 162°, $[\alpha]_D^{23}$ $-64·3°$ (*c* 0·5 in pyridine), $-52·4°$ (*c* 0·5 in MeOH) (Found: N, 2·7%).

[6] Weygand, *Ber.*, 1939, **72**, 1666; Honeyman and Tatchell, *J.*, 1950, 967.

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N-p-*Nitrophenyl-α- and -β-D-glucosylamine.*—An about 1 : 1 anomeric mixture of α- and β-*N-p*-nitrophenyl-D-glucosylamine tetra-acetate (8·0 g.) was deacetylated in methanol (15 ml.) and N-sodium methoxide (1·5 ml.). Crystallisation occurred immediately after dissolution. The mixture was left overnight at room temperature. The precipitated crystals (3·65 g., 71%), $[\alpha]_D^{22}$ −74·6° (*c* 0·5 in pyridine), were extracted twice with hot ethanol. The insoluble pure β-anomer (2·4 g., 47%) had m. p. 184°, $[\alpha]_D^{22}$ −189° ⟶ −204° (*c* 0·5 in pyridine), −165° (*c* 0·2 in MeOH) {lit.,[9] m. p. 183°, $[\alpha]_D$ −192°, −193° ⟶ −202°, −200° (in pyridine)}.

The mother-liquor was treated with ether (150 ml.) and light petroleum (300 ml.); there separated a deacetylated product rich in the α-anomer (1·13 g., 22%), $[\alpha]_D^{22}$ +233° (*c* 0·5 in MeOH), m. p. 167° (decomp.).

Recrystallised from a little anhydrous methanol, this gave a product (30%) of m. p. 174°, $[\alpha]_D^{22}$ +337° (*c* 0·5 in MeOH), ⟶ −67° (in MeOH–HCl in 5 min.), +288° (*c* 0·5 in pyridine) (Found: C, 47·5; H, 5·2; N, 9·3. Calc. for $C_{12}H_{16}N_2O_7$: C, 48·0; H, 5·4; N, 9·3%).

In another experiment, with the same anomeric acetate as starting material, filtering the first precipitate after 15 min. gave a better yield of the α-anomer (35%), m. p. 160°, $[\alpha]_D^{22}$ +235° (*c* 0·5 in pyridine); a second precipitate (0·12 g., 9·4%) was almost pure α-anomer, m. p. 164°, $[\alpha]_D^{22}$ +252° (*c* 0·5 in pyridine), +291° (*c* 0·5 in MeOH).

The α- and β-anomers did not mutaroate in anhydrous methanol, even in 168 hr. On the addition of hydrochloric acid, they reached $[\alpha]_D$ −66° and −68°, respectively, which shifted within a few days towards 0° and to positive values as a consequence of hydrolysis.

N-p-*Nitrophenyl-α-D-glucosylamine Tetra-acetate.*—Almost pure *N-p*-nitrophenyl-α-D-glucosylamine, $[\alpha]_D$ +235° (in pyridine), with acetic anhydride in pyridine gave a product (85%), m. p. 142°, $[\alpha]_D^{21}$ +273° (*c* 0·5 in MeOH), +248° (*c* 0·5 in pyridine). This was recrystallised from a ten-fold quantity of ethanol–ether by addition of light petroleum. The needles produced had m. p. 153°, $[\alpha]_D^{22}$ +310° (*c* 0·5 in MeOH); mutarotation occurred in 5 min. in the presence of hydrochloric acid, giving $[\alpha]_D^{22}$ +271° (*c* 0·5 in pyridine) (Found: N, 5·9%) {lit.,[5,6] m. p. 168°, $[\alpha]_D$ +229·2° (in MeOH), +206·2° (in pyridine)}.

N-p-*Sulphamoylphenyl-α-D-glucosylamine.*—*N-p*-Sulphamoylphenyl-D-glucosylamine tetra-acetate (1·0 g.; containing about 83% of α-anomer), $[\alpha]_D$ +155° (in pyridine), was deacetylated in methanol (3 ml.) by means of N-sodium methoxide (0·3 ml.). The material dissolved at room temperature, and the small amount {0·08 g.; $[\alpha]_D$ −82° (in pyridine)} precipitated by the next day was filtered off. Ether (20 ml.) was added to the mother-liquor. The amorphous precipitate was dissolved in cold methanol and filtered from the insoluble residue {0·06 g.; $[\alpha]_D$ −99·5° (in pyridine); m. p. 195° (decomp.)}. The methanolic solution was mixed with ether (15 ml.). The amorphous, sticky material then precipitated was again filtered off, and finally light petroleum (20 ml.) was added. A solid (0·35 g., 52%) was precipitated on storage at 0° overnight, that was partly crystalline. This was extracted with ten parts of cold methanol. The residue (0·15 g. from 0·25 g.) had m. p. 189° (decomp.), $[\alpha]_D^{21}$ +182° (*c* 1 in pyridine), and, recrystallised from methanol, m. p. 189° (decomp.), $[\alpha]_D^{23}$ +184° (*c* 0·5 in MeOH), +182° (*c* 0·5 in pyridine) (Found: N, 8·1%).

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[9] Bognár and Nánási, *J.*, 1955, 189; Bognár and Nánási, *Magyar Kém. Folyóirat*, 1956, **62**, 90; also Weygand *et al.*, ref. 1.

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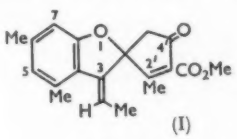
59. *Spirans. Part III.* The Structure and Stereochemistry of the Ozonolysis Products of 3-Alkylidenegris-2′-en-4′-ones.*

By F. M. Dean, D. S. Deorha, J. C. Knight, and Thomas Francis.

Oxidation of 3-alkylidenegris-2′-en-4′-ones (related to griseofulvin) by osmium tetroxide gives products which can be converted into the compounds previously obtained from abnormal ozonolyses of the same grisens. The structures (as IV) assigned to the ozonolysis products have thereby been confirmed: related studies have clarified the chief stereochemical features of these compounds, together with the nature of an unusual base-catalysed epimerisation which occurs in this series.

Improvements in the methods of synthesis of starting materials required in these and cognate studies are discussed.

In the usnolic acid series, spirans (I) are attacked by ozone in the expected fashion to give coumaranones (II), but in the grisan series ozonolysis (in methyl acetate) of spirans (III) gives anomalous results, the products having been assigned structures of type (IV). It is now shown that alcohols of general structures (VI) and (VII) can be prepared in both series by oxidising the appropriate spirans with osmium tetroxide. On the one hand, the alcohols can be methylated to products previously obtained by ozonolysis, thus confirming their structures, and on the other hand they possess a reactive centre (the hydroxyl group) useful in defining the stereochemistry of the tetracycles.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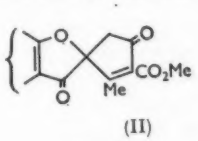
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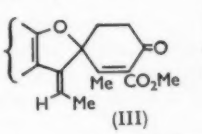
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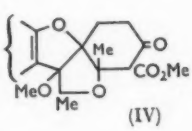
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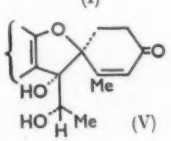
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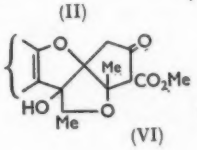
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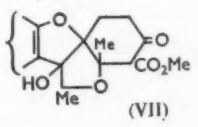
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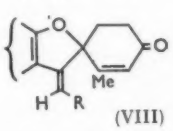
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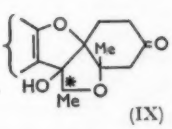
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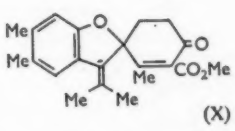

(X)

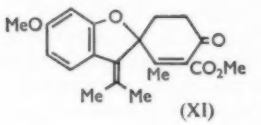
That the addition of osmium tetroxide to spirans of types (I) and (III) occurs, as expected, at the exocyclic double bonds appears from the fact that the adducts retain the spectroscopic characteristics of cyclohexenones. Reduction of the adducts by sulphur dioxide or by hydrogenation led, not to glycols [as (V)], but to isomers inert to periodates and having the more obvious properties of β-oxo-esters. Thus oxidation of the cyclopentenone ester (I) gave the tetracyclic alcohol (VI), and of the ring-homologue (III), gave an analogous alcohol (VII). While the chemical properties and ultraviolet absorption data for the alcohol (VII) were satisfactorily similar to those of the corresponding ozonolysis product (IV), correlations of infrared spectra were obscured by the avidity with which this alcohol (VII) retains methanol and ethanol, the solvents best suited to its preparation and purification. The ethanol could not be removed from the solvated methyl ester (VII) without destroying the crystalline form; and the ethanol solvate of the corresponding ethyl ester behaved similarly. Fortunately the methanol solvate of the ester (VII) could be converted into the solvent-free compound without loss of crystallinity, and the product,

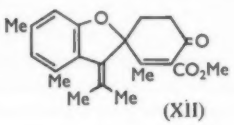
* Part II, *J.*, 1958, 4551.

whether examined in mulls or in solution, did not exhibit infrared carbonyl absorption characteristic of the non-enolic tautomer though it developed this when examined as a supercooled melt. This completed the analogy with the behaviour of the ozonolysis product (IV).

Oxidation of the grisen (VIII; R = Me) by osmium tetroxide furnished the tetracyclic saturated ketone (IX) which had $\nu_{max.}$ 3440 (OH) and 1720 cm.$^{-1}$ (C:O) and formed a 2,4-dinitrophenylhydrazone with $\lambda_{max.}$ 361 mμ (log ε 4·39). This ketone did not form stable solvates and when methylated in nearly neutral media (silver oxide and methyl iodide in dimethylformamide) supplied an ether identical with that obtained previously by ozonolysis of a ketone (III; H for CO_2Me). The suggested structures for the ozonolysis products are therefore confirmed, and it follows that the stereochemistry of these tetracyclic compounds is the same whichever method of oxidation is employed.

Theoretically, spirans such as (I) and (III) can also exist as the geometrical isomers, models showing, however, that in these isomers the methyl groups at the 4-position and on the exocyclic double-bond collide severely. This is clearly responsible for the fact that the


(XI)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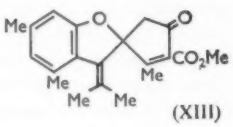
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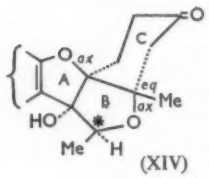
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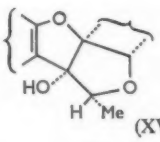
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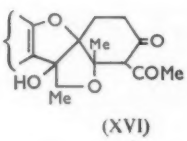
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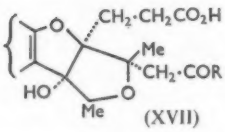
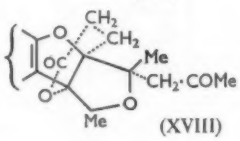

(XVII)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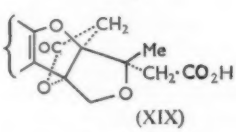
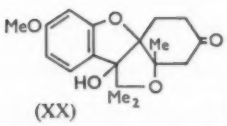
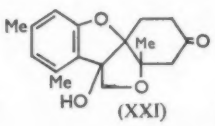
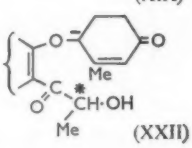

(XIX)


(XX)


(XXI)


(XXII)

(XXIII)

(XXIV)

spirans [I, III, VIII (R = H or Me), X, XI] may be made in good yield by the cyclisation of diketones such as (XXX), whereas spirans (XII) and (XIII), in which collision of methyl groups is unavoidable, cannot be made by this method.

Osmium tetroxide, being a bulky reagent, normally adds to the less hindered side of an ethylene; so the grisen (VIII; R = Me) can be assumed to afford a glycol (V), the dotted bonds lying towards the rear of the plane of the benzene ring. Axial attack by the (secondary) hydroxyl group occurring at the cyclohexenone double bond would accord with accepted views and result in a tetracycle (IX) of configuration (XIV) having the cyclohexanone ring in a favourable conformation, that is, with the phenoxide oxygen atom in the axial position. [In (XIV), the dotted lines refer to the conformation about ring B, the letters *ax* and *eq* to the conformation about the cyclohexanone ring.] It follows that both the A/B and the B/C ring-fusions are *cis*.

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To show that the A/B ring-fusion is indeed *cis*, the tetracyclic ester (VI) and also the tetracyclic ketone (XVI), obtained from osmium tetroxide and the ketone (III; COMe for CO_2Me), were hydrolysed by alkali. The latter hydrolysis gave a ketonic acid which, though it had properties consistent with structure (XVII; R = Me), did not crystallise and was therefore converted by heat into the ketonic δ-lactone (XVIII) with $\nu_{max.}$ 1761 * and 1706 cm.$^{-1}$. The ester (VI) supplied what seemed to be a dibasic acid but this could not be fully characterised because it so easily changed into the γ-lactonic acid (XIX), the methyl ester of which had $\nu_{max.}$ 1786 and 1738 cm.$^{-1}$. Both lactones had unexpectedly high lactonic carbonyl frequencies, but it seemed that neither could have been formed at all had the A/B ring-fusion been *trans*. Further work invalidated this simple argument.

The osmium tetroxide oxidation product (IX) isomerised in warm alkali and, as the corresponding methyl ether (IX; OMe for OH) was unaffected, the hydroxyl group must be essential to this change. The new isomer gave a different methyl ether isomeric with the ozonolysis product (IV; H for CO_2Me), and was so closely similar to the original alcohol in both chemical and spectroscopic properties that the change was thought to be stereochemical rather than structural in origin. This view was substantiated and the centre involved shown to be that starred in (IX) by the fact that neither compound (XX) nor (XXI) [obtained from the appropriate grisens (XI; H for CO_2Me) and (VIII; R = H) by the use of osmium tetroxide] was affected by alkali even in very vigorous conditions. Bases would of course induce β-elimination in (XIV), so that the tetracycles would revert to the glycols [as (V)], but in itself this provides no explanation of the above results. In the glycol (V), however, the presence of the tertiary alcohol group (but not, of course, of a methoxyl group) allows a reversed aldol condensation generating—if only momentarily—an intermediate (XXII) in which the starred centre is optically sensitive, so that when the rings close again the more stable of the two structures (XIV) and (XV) would be favoured. The benzene ring eclipses the methyl group at the atom starred in (XIV) but the resulting repulsion is absent from the epimer (XV), so that with (XV) as the structure of the new isomer all the facts can be satisfactorily explained.

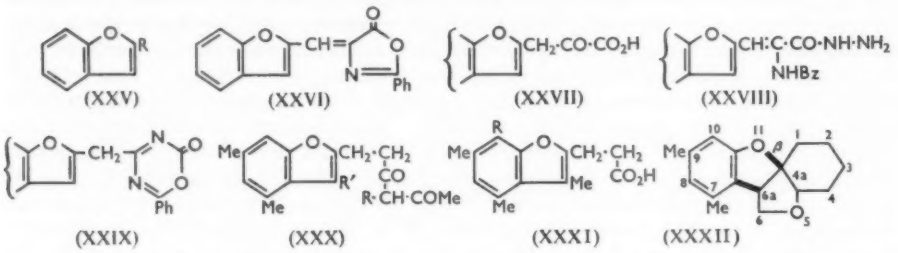
The above discussion destroys the chemical evidence adduced for the A/B *cis*-fusion, because the changes involved would allow an initial A/B *trans*-fused system to take up the *cis*-fused arrangement. Fortunately, there is considerable evidence that *cis*-fused tetrahydrofuran rings are nearly strain-free whereas *trans*-fused rings are strained. For example, lignans of type (XXIII) are invariably *cis*-fused, all attempts to prepare the corresponding *trans*-fused systems having failed.[1] The same considerations apply to the skeleton (XXIV), though there is a single instance of *trans*-fusion here.[2] In the present case, one tetrahydrofuran ring is modified by inclusion of a benzenoid double bond, models showing clearly that the strain in the *trans*-fused system is thereby greatly increased while the *cis*-fused system is not much affected. For these reaons it is very probable that, had compounds (XX) and (XXI) had A/B *trans*-fusion, treatment with alkali would have allowed them to attain the more stable A/B *cis*-fusion. As neither compound was affected by alkali even in forcing conditions, they must have been *cis*-fused in the first place. Consequently, expressions such as (XIV) may still be regarded as correct descriptions of the stereochemistry in the tetracyclic compounds.

As before, the acids of type (XXV; R = $CH_2 \cdot CO_2H$ or $CH_2 \cdot CH_2 \cdot CO_2H$) required for these and related studies were made from benzofurans (XXV; R = H) which were first converted into the aldehydes (XXV; R = CHO). The Gattermann reaction and the

* A Referee pointed out that this value is higher than those for most strain-free δ-lactones. We consider that the environment of the lactone ring is responsible for this because (XIX), undoubtedly a γ-lactone, also has an unusually high absorption frequency (1786 cm.$^{-1}$) compared with other members of its class. In the absence of suitable authentic model compounds, the matter cannot be pursued further at present.

[1] Hearon and MacGregor, *Chem. Rev.*, 1955, **55**, 959; Freudenberg and Fischer, *Chem. Ber.*, 1956, **89**, 1230; Beroza and Schechter, *J. Amer. Chem. Soc.*, 1956, **78**, 1242.
[2] Owen and Peto, *J.*, 1955, 2382; Ali and Owen, *J.*, 1958, 1074.

method [1] explored by Bisagni, Buu-Hoï, and Royer [3] were both used for this conversion and found to give comparable yields. The latter being much the more convenient, it is now preferred (see next section). 2-Benzofurylacetic acids (XXV; R = $CH_2 \cdot CO_2H$) were previously made from the aldehydes (XXV; R = CHO) by hydrolysis of the derived azlactones (XXVI) to the pyruvic acids (XXVII) and oxidation. This method has been compared with that introduced by Jennings.[4] In this, the azlactones (XXVI) are converted into the hydrazides (XXVIII) which, treated with nitrous acid and heated, form oxadiazines (XXIX) that furnish the furylacetic acids when hydrolysed. Again the two methods gave comparable yields, but that of Jennings was much the more expeditious in spite of the greater number of steps involved (see next section).



None of the methods described in Part II supplied acceptable yields of grisens of type (VIII). To remedy this, the acids (XXV; R = $CH_2 \cdot CO_2H$ or $CH_2 \cdot CH_2 \cdot CO_2H$), as their acid chlorides, were condensed with t-butyl acetoacetate to give dioxo-esters, *e.g.*, (XXX; R = CO_2Bu^t) which were easily transformed by toluene-*p*-sulphonic acid in hot toluene into crystalline diketones, *e.g.*, (XXX; R = H), the reaction being readily followed by the evolution of carbon dioxide. Cyclisation of the diketones then gave the desired grisens in good yield. Attempts to contract this sequence into one step by treating the ester (XXX; R = CO_2Bu^t) itself with sulphuric acid led chiefly to the acid (XXXI; R = Bu^t). The same compound was produced when the propionic acid (XXXI; R = H) was warmed with sulphuric acid and t-butyl alcohol, and is assigned the orientation written because steric hindrance would prevent entry of a t-butyl substituent between two methyl groups.

We have adopted the Editor's suggestions that, for the purpose of systematic nomenclature, the Ring Index method be applied and rings B and C of the tetracyclic spirans be regarded as contained in the plane of the paper, with the bond to the phenoxide oxygen atom rising from this plane and given the arbitrary stereochemical designation β as in (XXXII). Thus compound (XIV) is named 2,3,4,4a,6,6a-hexahydro-6aα-hydroxy-4aβ,6β,7,9-tetramethyl-3-oxo-1*H*-5,11-dioxadibenzo[*a*,*d*]pentalene; compound (VI) is named methyl 1,2,3,3a,5,5a-hexahydro-5a-hydroxy-3a,5,6,8-tetramethyl-2-oxo-4,10-dioxabenzo[*a*]cyclopenta[*d*]pentalene; and compound (XVII; R = OH) is named 3aα-2′-carboxyethyl-3α-carboxymethyl-8bα-hydroxy-1,3,3a,8b-tetrahydro-1,3β,6,8-tetramethyl-2,4-dioxacyclopenta[*a*]indene.

Experimental

2-*Hydroxy*-4,5-*dimethylisobutyrophenone*.—3,4-Dimethylphenyl isobutyrate (60 g.), kept with aluminium chloride (60 g.) at 130° for 5 hr., formed an orange complex which was decomposed with ice and hydrochloric acid. The product, isolated with ether, was purified by distillation, giving the *isobutyrophenone*, b. p. 150°/20 mm., with a purple ferric reaction (Found: C, 74·8; H, 8·3. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·4%). The *oxime* separated from benzene in prisms, m. p. 136° (Found: N, 6·9. $C_{12}H_{17}NO_2$ requires N, 6·8%).

[3] Bisagni, Buu-Hoï, and Royer, *J.*, 1955, 3688.
[4] Jennings, *J.*, 1957, 1512.

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2-Isobutyryl-3,5-dimethylphenoxyacetic Acid.—A mixture of 2-hydroxy-4,6-dimethylisobutyrophenone [5] (100 g.), potassium carbonate (85 g.), ethyl bromoacetate (96 g.), and acetone (500 ml.) was kept at the b. p. for 20 hr. Evaporation of the hot filtrate left an oil which solidified and, when purified from light petroleum (b. p. 40—60°), supplied *ethyl 2-isobutyryl-3,5-dimethylphenoxyacetate* in needles (140 g.), m. p. 67° (Found: C, 68·8; H, 7·9. $C_{16}H_{22}O_4$ requires C, 69·0; H, 8·0%). This ester (70 g.) was heated with sodium hydroxide (40 g.) in alcohol (200 ml.) and water (200 ml.) until it all dissolved (about 1 hr.). After the cooled solution had been made up to 2 l. with water, addition of concentrated hydrochloric acid liberated the *phenoxyacetic acid* which separated from benzene–light petroleum in needles (60 g.), m. p. 138° (Found: C, 67·3; H, 7·2. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%).

2-Isobutyryl-5-methoxyphenoxyacetic Acid.—2-Hydroxy-4-methoxyisobutyrophenone [6] (97 g.) was etherified by ethyl bromoacetate as in the foregoing experiment. The oily phenoxyacetate was not purified but was hydrolysed at once to the *phenoxyacetic acid* which separated from benzene in rods (112 g.), m. p. 108° (Found: C, 61·6; H, 6·5; OMe, 12·2. $C_{12}H_{13}O_4 \cdot OMe$ requires C, 61·9; H, 6·4; OMe, 12·3%).

2-Isobutyryl-4,5-dimethylphenoxyacetic Acid.—Prepared from 2-hydroxy-4,5-dimethylisobutyrophenone by the method described above, this *dimethylphenoxyacetic acid* crystallised from benzene in rhombs, m. p. 118° (Found: C, 67·2; H, 7·2. $C_{14}H_{18}O_4$ requires C, 66·9; H, 7·3%).

2-Isobutyryl-4-methylphenoxyacetic Acid.—Obtained by the same method as the above phenoxy-acids, *2-isobutyryl-4-methylphenoxyacetic acid* formed needles, m. p. 106°, when purified from light petroleum (b. p. 40—60°) (Found: C, 65·9; H, 7·0. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%).

4-Chloro-3,5-dimethyl-2-propionylphenoxyacetic Acid.—Interaction of 3-chloro-6-hydroxy-2,4-dimethylpropiophenone [7] and ethyl bromoacetate by the usual method gave *ethyl 4-chloro-3,5-dimethyl-2-propionylphenoxyacetate* which crystallised from light petroleum (b. p. 40—60°) in needles, m. p. 60° (Found: C, 60·4; H, 6·6. $C_{15}H_{19}O_4Cl$ requires C, 60·3; H, 6·4%). Alkaline hydrolysis supplied the *phenoxyacetic acid* which crystallised from benzene in needles, m. p. 162° (Found: C, 57·4; H, 5·7. $C_{13}H_{15}O_4Cl$ requires C, 57·6; H, 5·5%).

2-Isobutyryl-5-methylphenoxyacetic Acid.—The standard procedure applied to 2-hydroxy-4-methylisobutyrophenone gave the desired *phenoxyacetic acid* as prisms, m. p. 92°, from benzene (Found: C, 66·1; H, 6·7. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%).

Benzofurans (XXV; R = H).—For the preparation of these, the *o*-acylphenoxyacetic acids (0·4 mole) were heated with sodium acetate (100 g.) and acetic anhydride (300 ml.) at 160° for 1 hr., cooled, and poured into water (2 l.). The oils produced were collected into ether, washed with aqueous sodium hydrogen carbonate to remove acids, dried ($MgSO_4$), and recovered by evaporation of the solvent. The crude *benzofurans* (see Table) were then purified by distillation and/or crystallisation.

Benzofurans (XXV; R = H).

Substituents	B. p./mm.	n_D/° c	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
3-Isopropyl-5-methyl	82°/0·5	1·5335/15·5	$C_{12}H_{14}O$	82·8	7·8	82·7	8·1
3-Isopropyl-6-methyl	78°/0·4	1·5345/20·0	$C_{12}H_{14}O$	82·7	8·1	82·7	8·1
3-Isopropyl-4,6-dimethyl * ...	97°/1·0	1·5412/17·0	$C_{13}H_{16}O$	82·9	8·8	83·0	8·6
3-Isopropyl-5,6-dimethyl	98°/0·7	1·5378/20	$C_{13}H_{16}O$	82·8	8·9	83·0	8·6
5-Chloro-3-ethyl-4,6-dimethyl	Plates, m. p. 45°, from light petroleum		$C_{12}H_{13}ClO$	68·8	6·1	69·1	6·2

* Prisms, m. p. 30°, from light petroleum.

2-Formylbenzofurans (XXV; R = CHO).—(i) To freshly distilled phosphorus oxychloride (1 mol.) mixed with dimethylformamide (1 mol.) at 5° was added a solution of the benzofuran (1 mol.) in dimethylformamide. The mixture was kept at 85° (60° for methoxybenzofurans) for 1 hr., cooled, diluted with water, and neutralised with sodium hydrogen carbonate. 2 Hr. later, the product was isolated with ether and purified by distillation or crystallisation from aqueous alcohol.

[5] von Auwers, *Annalen*, 1920, **421**, 74.
[6] Dohme, Cox, and Miller, *J. Amer. Chem. Soc.*, 1926, 1692; Reichstein, Oppenauer, Grüssner, Hirt, Rhyner, and Glatthaar, *Helv. Chim. Acta*, 1935, **18**, 816.
[7] Tiwari and Singh, *J. Indian Chem. Soc.*, 1958, **35**, 749.

XUM

2-Formylbenzofurans (XXV; R = CHO).

No.	Substituents	B. p./mm. or m. p.	Yield (%) (i)	Yield (%) (ii)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
(1)	3,4,6-Trimethyl [a]		85	85					
(2)	3-Ethyl-4,6-dimethyl [a]		82	86					
(3)	3-Isopropyl-5-methyl	150°/2·0	34	36	$C_{13}H_{14}O_2$	77·2	7·1	77·2	7·0
(4)	3-Isopropyl-6-methyl	150°/3·0	83	81	$C_{13}H_{14}O_2$	77·4	7·1	77·2	7·0
(5)	3-Isopropyl-4,6-dimethyl	159°/3	84	86	$C_{14}H_{16}O_2$	77·7	7·5	77·8	7·4
(6)	3-Isopropyl-5,6-dimethyl *	122°	48	50	$C_{14}H_{16}O_2$	77·5	7·6	77·8	7·4
(7)	5-Chloro-3-ethyl-4,6-dimethyl	124°	42	43	$C_{12}H_{13}ClO_2$	65·7	5·3	66·0	5·5
(8)	3-Isopropyl-6-methoxy †	154°/1·0	78	80	$C_{13}H_{14}O_3$	71·4	6·4	71·5	6·5

* Pure specimens could be obtained only by hydrolysis of the semicarbazone, which separated from aqueous alcohol in flakes, m. p. 238° (Found: N, 15·1. $C_{15}H_{19}N_3O_2$ requires N, 15·4%).

† M. p. 30° (Found: OMe, 14·5. $C_{12}H_{11}O_2$·OMe requires OMe, 14·2%). Aluminium chloride was omitted from this preparation.

2-Formylbenzofuran 2,4-dinitrophenylhydrazones.

No.*	M. p.	Colour	Formula	Found (%)	Required (%)
3	218°	Red	$C_{19}H_{18}N_4O_5$	14·3	14·7
4	226	Red	$C_{19}H_{18}N_4O_5$	14·4	14·7
5	250	Scarlet	$C_{20}H_{20}N_4O_5$	14·0	14·1
6	294	Orange	$C_{20}H_{20}N_4O_5$	14·0	14·1
7	246	Red	$C_{19}H_{17}ClN_4O_5$	13·2	13·4
8	228	Maroon	$C_{19}H_{18}N_4O_6$	14·1	14·1

* See preceding Table.

These *aldehydes* (see Table) gave *2,4-dinitrophenylhydrazones* as tabulated.

(ii) A solution of the benzofuran (0·2 mole) in ether (400 ml.) containing hydrogen cyanide (18 ml.) and aluminium chloride (34 g.) was saturated with hydrogen chloride at 0°. Next day, volatile materials were allowed to escape and the residue was added to water (2 l.): when the vigorous reaction had subsided the water was boiled to complete the hydrolysis. A heavy oil separated and was taken up in ether, washed with aqueous sodium hydrogen carbonate, dried ($MgSO_4$), recovered by evaporation of the solvent, and purified by distillation or other appropriate method.

Azlactones (XXVI).—The 2-formylbenzofuran (0·2 mol.) was heated with hippuric acid (70 g.), sodium acetate (40 g.), and acetic anhydride (250 ml.) on the steam-bath for 2 hr. The cooled product was diluted with 50% alcohol (700 ml.) and kept overnight to complete the precipitation of the *azlactone*, which was then collected and crystallised from alcohol (see Table).

4-2′-Benzofurylmethylene-2-phenyloxazolin-5-ones (XXVI).

Substituents	M. p.	Habit	Formula	Found N (%)	Required N (%)
3-Isopropyl-6-methyl	176°	Yellow needles	$C_{22}H_{19}NO_3$	4·0	4·1
3-Isopropyl-4,6-dimethyl	228	Yellow prisms	$C_{23}H_{21}NO_3$	4·0	3·9
5-Chloro-3-ethyl-4,6-dimethyl	216	Yellow needles	$C_{22}H_{18}ClNO_3$	3·4	3·7
3-Isopropyl-6-methoxy	160	Golden needles	$C_{22}H_{19}NO_4$	3·6	3·9

Pyruvic Acids (XXVII).—The azlactone (0·09 mole) was boiled with 20% aqueous potassium hydroxide (300 ml.) until ammonia was no longer evolved, water being added intermittently to maintain the volume of fluid. The resulting solution, diluted with water (750 ml.) and acidified with concentrated hydrochloric acid, was warmed to 60° to coagulate the precipitate which had been formed. The solid was collected, washed with warm water, and crystallised from aqueous alcohol to give the *pyruvic acid* (see Table).

2′-Benzofurylpyruvic acids (XXVII).

Substituents	M. p.	Habit	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
3-Isopropyl-6-methyl	184°	Yellowish needles	$C_{15}H_{16}O_4$	69·3	6·3	69·2	6·2
3-Isopropyl-4,6-dimethyl	192	Yellowish needles	$C_{16}H_{18}O_4$	70·1	6·3	70·1	6·6
5-Chloro-3-ethyl-4,6-dimethyl	210	Pinkish needles	$C_{15}H_{15}ClO_4$	60·8	4·9	61·1	5·1
3-Isopropyl-6-methoxy	165	Yellowish plates	$C_{15}H_{16}O_5$	64·9	5·7	65·2	5·8

[a] Dean, Halewood, Mongkolsuk, Robertson, and Whalley, *J.*, 1953, 1250.

XUM

Hydrazides (XXVIII).—The finely powdered azlactone (0·02 mole), suspended in ether (150 ml.), was treated with hydrazine hydrate (0·028 mole) and stirred until the colour was completely discharged; the resulting solid was collected and purified from alcohol. All the *hydrazides* obtained thus (see Table) formed needles.

α-Benzamido-β-2-benzofurylacrylohydrazides (XXVIII).

Substituents	M. p.	Formula	Found N (%)	Required N (%)
3-Ethyl-4,6-dimethyl	198°	$C_{23}H_{23}N_3O_3$	11·0	11·1
3-Isopropyl-6-methyl	184	$C_{23}H_{23}N_3O_3$	11·2	11·1
3-Isopropyl-4,6-dimethyl	180	$C_{23}H_{25}N_3O_3$	10·6	10·7
5-Chloro-3-ethyl-4,6-dimethyl	212	$C_{23}H_{22}ClN_3O_3$	10·1	10·3
3-Isopropyl-6-methoxy	186	$C_{23}H_{23}N_3O_4$	10·8	10·7
4,6-Dimethoxy-3-methyl	230	$C_{21}H_{21}N_3O_5$	10·5	10·6

Oxadiazines (XXIX).—A solution of sodium nitrite in the minimum amount of water was added slowly to the hydrazide (XXVIII) in the smallest convenient quantity of acetic acid, the temperature being kept below 17°. After ½ hr., the yellow crystalline precipitate was washed with water, to give crude azides which were too unstable for characterisation. The azides were dried in air and extracted from a Soxhlet thimble with benzene. When concentrated and cooled, the benzene extracts deposited the *oxadiazines* (XXIX) (see Table) which usually formed needles when recrystallised from benzene.

4-2′-Benzofuryl-6-phenyl-1,3,5-oxadiazin-2-ones (XXIX).

Substituents	Colour	M. p.	Formula	Found N (%)	Required N (%)
3-Ethyl-4,6-dimethyl	Red	174°	$C_{23}H_{20}N_2O_3$	7·7	7·8
3-Isopropyl-6-methyl	Deep yellow	206	$C_{23}H_{20}N_2O_3$	7·6	7·8
3-Isopropyl-4,6-dimethyl	Yellow rods	226	$C_{25}H_{24}N_2O_3$	7·3	7·5
5-Chloro-3-ethyl-4,6-dimethyl	Orange-red	246	$C_{25}H_{19}ClN_2O_3$	6·8	7·1
3-Isopropyl-6-methoxy	Orange-yellow	208	$C_{25}H_{20}N_2O_4$	7·2	7·4
4,6-Dimethoxy-3-methyl	Red	226	$C_{21}H_{18}N_2O_5$	7·2	7·4

2-Benzofurylacetic Acids (XXV; R = $CH_2{\cdot}CO_2H$).—(i) Hydrogen peroxide (100-vol.; 20 ml.) was added to the pyruvic acid (0·062 mole) in 5% aqueous potassium hydroxide (20 ml.) at 0°. After 5 min. the mixture was diluted with iced water (1 l.) and acidified with dilute sulphuric acid to liberate the crude 2-benzofurylacetic acid which was crystallised from light petroleum or from aqueous alcohol (see Table).

(ii) A mixture of the oxadiazine (0·1 mole), acetic acid (400 ml.), and dilute hydrochloric acid (40 ml.) was boiled until dissolution was complete and the colour was discharged, whereafter dilution with water precipitated the benzofurylacetic and benzoic acids. The latter was leached out with water at 60°, leaving the crude benzofurylacetic acid which was recrystallised from light petroleum or aqueous alcohol.

2-Benzofurylacetic acids.

Substituents	M. p.	Yields * (%) (i)	(ii)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
3-Ethyl-4,6-dimethyl [9]		54	56					
3-Isopropyl-6-methyl	136°	55	55	$C_{14}H_{16}O_3$	72·2	6·6	72·4	6·9
3-Isopropyl-4,6-dimethyl	158	50	48	$C_{15}H_{18}O_3$	73·0	7·3	73·1	7·4
5-Chloro-3-ethyl-4,6-dimethyl	182	57	55	$C_{14}H_{15}ClO_3$	63·1	5·8	63·0	5·5
3-Isopropyl-6-methoxy	142	51	49	$C_{14}H_{16}O_4$	67·7	6·3	67·7	6·5
4,6-Dimethoxy-3-methyl [9]		50	52					

* Overall yields based on 2-formylbenzofurans.

3-Isopropyl-6-methoxybenzofuran-2-carboxylic Acid.—These reactions were carried out to ensure that 2-formyl-3-isopropyl-6-methoxybenzofuran, prepared as above, had the formyl group in the 2-position.[9]

(i) 2-Formyl-3-isopropyl-6-methoxybenzofuran (1 g.) in acetone (30 ml.) was oxidised by potassium permanganate (0·6 g.) in the least quantity of water. 18 Hr. later, the mixture was clarified by sulphur dioxide and diluted with water. The precipitate, taken up in ether and

[9] Birch and Robertson, *J.*, 1938, 306.

extracted thence into aqueous sodium hydrogen carbonate, was liberated by acidification and crystallised from acetic acid, giving the methoxybenzofuran-2-carboxylic acid in prisms, m. p. 180° (lit., m. p. 180°). (ii) The crude phenoxyacetate (1 g.) formed as an intermediate in the preparation of 2-isobutyryl-5-methoxyphenoxyacetic acid (see above) was heated with a solution from sodium (0·2 g.) in alcohol (10 ml.) on the steam-bath for 15 min. The product was isolated by dilution with water (20 ml.) and acidification, and when purified from glacial acetic acid gave the methoxybenzofuran-2-carboxylic acid in prisms, m. p. 180°, identical with a sample prepared by method (i).

3-Isopropyl-4,6-dimethylbenzofuran-3-carboxylic Acid.—Prepared by both the methods described for the 6-methoxybenzofuran-3-carboxylic acid analogue, *3-isopropyl-4,6-dimethylbenzofuran-2-carboxylic acid* separated from acetic acid in prisms, m. p. 232° (Found: C, 72·2; H, 6·8. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%).

β-(3-Isopropyl-4,6-dimethyl-2-benzofuryl)propionic Acid.—When effervescence ceased in a mixture of 2-formyl-3-isopropyl-4,6-dimethylbenzofuran (50 g.), malonic acid (50 g.), piperidine (1 ml.), and pyridine (150 ml.) held at 100°, a large excess of dilute hydrochloric acid was added. The reddish precipitate was collected, washed with water, and dried in air before being boiled with benzene (100 ml.) to extract impurities. The white residue crystallised from a large volume of benzene to give *β-(3-isopropyl-4,6-dimethyl-2-benzofuryl)acrylic acid* in needles (48 g.), m. p. 230° (decomp.), $\lambda_{max.}$ 248, 336 mμ (log ε 3·80, 4·52) (Found: C, 74·2; H, 7·0. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%). Suspended in 10 : 1 ether–methanol and treated with diazomethane until no more effervescence was noted, this acrylic acid furnished the *methyl ester*, which separated from aqueous methanol in needles, m. p. 45° (Found: OMe, 11·7. $C_{16}H_{17}O_2{\cdot}OMe$ requires OMe, 11·4%).

The acrylic acid (12 g.) in 0·1N-aqueous sodium hydroxide (500 ml.) containing Raney nickel (1·5 g.) was shaken with hydrogen (50 atm.) for 6 hr. The oil that separated when the filtrate was acidified solidified slowly and was then purified from light petroleum (b. p. 40—60°), giving the *propionic acid* in prisms (10 g.), m. p. 76°, $\lambda_{max.}$ 258, 296 mμ (log ε 4·16, 3·42). This substance retained the solvent tenaciously, and had to be melted before consistent analytical data could be obtained (Found: C, 74·0; H, 7·8. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%). The *methyl ester*, prepared by means of diazomethane, was an oil, b. p. 190°/1 mm. (Found: OMe, 11·3. $C_{16}H_{19}O_2{\cdot}OMe$ requires OMe, 11·3%), but the *hydrazide*, prepared from this ester and hydrazine hydrate, crystallised from aqueous methanol in plates, m. p. 141° (Found: N, 10·2. $C_{16}H_{22}N_2O_3$ requires N, 10·2%).

β-(3,4,6-Trimethyl-7-t-butyl-2-benzofuryl)propionic Acid (XXXI; R = Bu^t).—β-(3,4,6-Trimethyl-2-benzofuryl)propionic acid (2·5 g.) was mixed with sulphuric acid monohydrate (30 ml.) and t-butyl alcohol (0·75 g.) and left at −2° for 2 days. After the addition of crushed ice, ether extracted material part of which was soluble in aqueous sodium hydrogen carbonate and was identified as the starting material; the insoluble part, when isolated by means of dilute sodium hydroxide solution and crystallised from aqueous alcohol, afforded the *t-butylbenzofurylpropionic acid* in needles (0·8 g.), m. p. 163° (Found: C, 74·8; H, 8·4; O, 16·3. $C_{18}H_{24}O_3$ requires C, 75·0; H, 8·4; O, 16·6%).

β-(3-Isopropyl-5,6-dimethyl-2-benzofuryl)propionic Acid.—Obtained from 2-formyl-3-isopropyl-5,6-dimethylbenzofuran by the method given above for the 4,6-dimethyl isomer, *β-(3-isopropyl-5,6-dimethyl-2-benzofuryl)acrylic acid* formed needles, m. p. 236°, when crystallised from benzene (Found: C, 74·4; H, 7·0. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%): the *methyl ester* separated from aqueous methanol in prisms, m. p. 85° (Found: OMe, 11·4. $C_{16}H_{17}O_3{\cdot}OMe$ requires OMe, 11·4%).

Hydrogenation of the acrylic acid on Raney nickel afforded the *propionic acid* which formed rods, m. p. 120°, from light petroleum (b. p. 60—80°) (Found: C, 73·7; H, 7·8. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%). The methyl ester prepared by means of diazomethane was an oil which was converted into the *hydrazide*, plates, m. p. 130° (from aqueous methanol) (Found: N, 10·4. $C_{16}H_{22}N_2O_3$ requires N, 10·2%).

β-(3-Isopropyl-5-methyl-2-benzofuryl)propionic Acid.—By the method described for the analogues, 2-formyl-3-isopropyl-5-methylbenzofuran was converted into *β-(3-isopropyl-5-methyl-2-benzofuryl)acrylic acid* which crystallised from benzene in needles, m. p. 230° (Found: C, 73·7; H, 6·7. $C_{15}H_{16}O_3$ requires C, 73·8; H, 6·6%), and with diazomethane rapidly gave the *methyl ester*, crystallising from aqueous methanol in needles, m. p. 70° (Found: C, 74·3; H, 7·1. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%).

XUM

Hydrogenation of the acrylic acid furnished the *propionic acid* which separated from light petroleum (b. p. 40—60°) in cubes, m. p. 97° (Found: C, 73·2; H, 7·5. $C_{15}H_{18}O_3$ requires C, 73·1; H, 7·4%), and formed a *methyl ester* as needles, m. p. 28°, from light petroleum (b. p. 40—60°) (Found: C, 73·9; H, 7·7. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%).

β-(3-*Isopropyl*-6-*methoxy*-2-*benzofuryl*)*propionic Acid*.—By interaction with malonic acid in hot pyridine containing piperidine, 2-formyl-3-isopropyl-6-methoxybenzofuran (20 g.) was converted into β-(3-*isopropyl*-6-*methoxy*-2-*benzofuryl*)*acrylic acid*, which, when purified from benzene (charcoal), formed cream needles (19 g.), m. p. 198°, $\lambda_{max.}$ 252, 340 mμ (log ε 3·79, 4·79) (Found: C, 69·1; H, 6·3; OMe, 12·0. $C_{14}H_{13}O_3$·OMe requires C, 69·2; H, 6·2; OMe, 11·9%). Hydrogenation of this acrylic acid on Raney nickel afforded the *methoxybenzofurylpropionic acid* as cubes, m. p. 76—78°, $\lambda_{max.}$ 249, 256, 292 mμ (log ε 4·12, 4·12, 3·81), from light petroleum (b. p. 40—60°) (Found: C, 68·7; H, 7·2; OMe, 12·1. $C_{14}H_{15}O_3$·OMe requires C, 68·7; H, 6·9; OMe, 11·8%).

4,6,2′-*Trimethyl*-3-*methylenegris*-2′-*en*-4′-*one* (VIII; R = H).—β-(3,4,6-Trimethyl-2-benzofuryl)propionic acid (10 g.) (Part II) was added to phosphorus pentachloride (10 g.) in chloroform (75 ml.). After ½ hr., the temperature was raised to 60° for ½ hr., and then the solvent was distilled off. Phosphorus oxychloride was removed by co-distillation with benzene, and the residual crude acid chloride was further purified by subjection to a vacuum at 50° for ½ hr. To the product in ether (125 ml.) was added the ethoxymagnesio-derivative (equiv. to 1·2 g. of magnesium) of t-butyl acetoacetate, and the mixture was heated under reflux for 3 hr. The resulting complex was decomposed by dilute acetic acid, and the organic layer, having been washed with sodium hydrogen carbonate solution and with water and dried ($MgSO_4$), was evaporated, leaving a crude dioxo-ester (XXX; R = CO_2Bu^t, R′ = Me) as a viscous oil with a pleasant odour and an intense red ferric reaction. This oil was warmed in toluene (150 ml.) containing toluene-*p*-sulphonic acid (0·5 g.) on the steam-bath until carbon dioxide was no longer evolved (about 3 hr.). When cool, the solution was diluted with ether, washed with aqueous sodium hydrogen carbonate and then water, dried ($MgSO_4$), and concentrated, finally under reduced pressure. The residue solidified and when purified first by chromatography from benzene on silica and then by crystallisation from light petroleum (b. p. 40—60°) supplied 5-(3,4,6-*trimethyl*-2-*benzofuryl*)*hexane*-2,4-*dione* (XXX; R = H, R′ = Me) in needles (4·4 g.), m. p. 83°, $\nu_{max.}$ 1639 cm.$^{-1}$ (broad: chelated carbonyl), with a red ferric reaction (Found: C, 74·7; H, 7·4. $C_{17}H_{20}O_3$ requires C, 75·0; H, 7·4%).

This diketone (2 g.), mixed at 5° with sulphuric acid monohydrate (15 ml.), was kept at −2° for 2 days, treated with crushed ice, and extracted with ether. Acidic materials were removed by means of 2N-sodium hydroxide, and the solution was then washed with water, dried ($MgSO_4$), and evaporated. The product solidified in contact with light petroleum (b. p. 60—80°) and when crystallised from this solvent afforded the *trimethyl*-3-*methylenegrisenone* in faintly yellow prisms (1·5 g.), m. p. 111°, insoluble in 2N-sodium hydroxide, devoid of a ferric reaction, and having $\nu_{max.}$ 1675 cm.$^{-1}$ (conj. ketone) [Found: C, 80·1; H, 7·2%; *M* (Rast), 215. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%; *M*, 254]. The 2,4-*dinitrophenylhydrazone* crystallised in orange needles, m. p. 208°, from ethyl acetate (Found: C, 63·5; H, 5·3; N, 12·8. $C_{23}H_{22}N_4O_5$ requires C, 63·6; H, 5·1; N, 12·9%).

When the crude dioxo-ester (5·0 g.) was treated directly with sulphuric acid monohydrate (15 ml.) at 5° (that is, with omission of the treatment with toluene-*p*-sulphonic acid), three products were formed. The neutral one was the desired grisen (0·25 g.), m. p. and mixed m. p. 111°; another, an acid insoluble in aqueous sodium hydrogen carbonate, was identified spectroscopically and by mixed m. p.s with the t-butylpropionic acid (XXXI; R = Bu^t); the third, an acid soluble in sodium hydrogen carbonate solution, was obtained in small yield only but is considered to be 4,6,2′-*trimethyl*-3-*methylene*-4′-*oxogris*-2′-*en*-3′-*carboxylic acid*: it separated from alcohol–light petroleum in needles, m. p. 150°, having an infrared spectrum closely similar to that of the 3-ethylidene homologue (Found: C, 72·6; H, 6·1%; *M*, 267. $C_{17}H_{17}O_2$·CO_2H requires C, 72·5; H, 6·1%; *M*, 298).

4,6,2′-*Trimethyl*-3-*ethylidenegris*-2′-*en*-4′-*one* (VIII; R = Me).—Prepared in the same way as the foregoing 3-methyl analogue but beginning with β-(3-ethyl-4,6-dimethyl-2-benzofuryl)-propionic acid (10 g.), 5-(3-*ethyl*-4,6-*dimethyl*-2-*benzofuryl*)*hexane*-2,4-*dione* (XXX; R = H, R′ = Et) was purified from benzene on silica and recrystallised from light petroleum (b. p. 40—60°) as plates (7·4 g.), m. p. 87° (Found: C, 75·6; H, 7·9. $C_{18}H_{22}O_3$ requires C, 75·5; H, 7·7%).

Cyclised by sulphuric acid monohydrate at −2° by the general method, the diketone (5 g.)

supplied the 3-ethylidenegrisenone which crystallised from light petroleum (b. p. 60—80°) in pale yellow prisms (1·2 g.), m. p. 106°, not depressed by admixture with specimens prepared by methods given in Part II.

Methyl 4,6,2′-Trimethyl-3-methylene-4′-oxogris-2′-en-3′-carboxylate.—The acid chloride from β-(3,4,6-trimethyl-2-benzofuryl)propionic acid (10 g.) interacted with the methoxymagnesio-derivative (20 g.) of methyl acetoacetate in boiling ether (200 ml.) during 3 hr. Isolated by evaporation of the ethereal layer obtained when dilute acetic acid was added, *methyl α-acetyl-β-oxo-δ-(3,4,6-trimethyl-2-benzofuryl)valerate* (XXX; R = CO_2Me, R′ = Me) crystallised from light petroleum (b. p. 40—60°) in pale yellow prisms (8 g.), m. p. 88° (Found: C, 68·9; H, 6·7. $C_{19}H_{22}O_5$ requires C, 69·1; H, 6·7%). Treated with sulphuric acid monohydrate (10 ml.) at 2° for 12 hr., this ester (1 g.) cyclised giving a gum, that was isolated by the addition of ice followed by extraction into ether. Acidic materials were removed from the extract by means of 2N-sodium hydroxide, whereafter evaporation of the solvent left a solid which, purified from aqueous alcohol, gave the *methyl 3-methyleneoxogrisencarboxylate* in needles (0·5 g.), m. p. 151° (Found: C, 73·0; H, 6·7; OMe, 9·8. $C_{15}H_{17}O_3$·OMe requires C, 73·1; H, 6·5; OMe, 9·9%).

3-Isopropylidene-6-methoxy-2′-methylgris-2′-en-4′-one (XI; H for CO_2Me).—β-(3-Isopropyl-6-methoxy-2-benzofuryl)propionic acid (5·2 g.) was converted into the acid chloride, condensed with t-butyl acetoacetate, and de-esterified by the method described for the analogues. The resulting crude β-diketone could not be properly purified and was therefore treated at once with sulphuric acid monohydrate (25 ml.) at 2°. After 2 days, the product was isolated in the usual fashion and formed an oil which solidified in contact with light petroleum (b. p. 60—80°) and was purified from benzene on a silica column. Thus obtained, the *isopropylidenemethoxygrisenone* separated from benzene–light petroleum (b. p. 60—80°) in pyramids (1·3 g.), m. p. 120°, $\lambda_{max.}$ 220, 228, 261, 312 mμ (log ε 4·45, 4·47, 4·20, 4·07), $\nu_{max.}$ 1670 cm.$^{-1}$ (cyclohexenone C:O) (Found: C, 75·9; H, 7·2. $C_{18}H_{20}O_3$ requires C, 76·0; H, 7·0%). Crystallised from alcohol, the 2,4-*dinitrophenylhydrazone* appeared as needles, m. p. 248° (Found: N, 12·2. $C_{24}H_{24}N_4O_6$ requires N, 12·1%).

Methyl 3-Isopropylidene-5,6,2′-trimethyl-4′-oxogris-2′-en-3′-carboxylate (X).—Interaction of β-(3-isopropyl-5,6-dimethyl-2-benzofuryl)propionic acid (5·2 g.) with phosphorus pentachloride (4·2 g.) in chloroform (20 ml.) at 50° for 1 hr. gave an acid chloride which was partially purified by repeated distillation with benzene and when condensed with the methoxymagnesio-derivative (5 g.) of methyl acetoacetate in boiling ether for 1 hr. supplied a complex salt. This, when decomposed by dilute acetic acid, afforded an oil which, after purification on silica from light petroleum followed by crystallisation from the same solvent (b. p. 40—60°), gave *methyl α-acetyl-δ-(3-isopropyl-5,6-dimethyl-2-benzofuryl)-β-oxovalerate* in yellow needles (5 g.), m. p. 63°, $\lambda_{max.}$ 260, 284 mμ (log ε 4·20, 4·18), $\nu_{max.}$ 1706, 1563 cm.$^{-1}$ (Found: C, 70·5; H, 7·3; OMe, 8·6. $C_{20}H_{24}O_4$·OMe requires C, 70·4; H, 7·3; OMe, 8·7%).

In sulphuric acid monohydrate (12 ml.) at 2° (2 days) the foregoing ester (4·0 g.) cyclised and the product was isolated by the addition of crushed ice followed by extraction into ether. The neutral fraction, when crystallised from aqueous methanol, supplied the *isopropylidenetrimethyloxogrisencarboxylate* in yellowish rods (1·3 g.), m. p. 160°, $\lambda_{max.}$ 216, 233, 260, 268, 317, 330 mμ (log ε 4·43, 4·45, 4·24, 4·13, 4·03, 4·06), $\nu_{max.}$ 1736 (ester), 1672 cm.$^{-1}$ (conjugated C:O), devoid of a ferric reaction (Found: C, 74·2; H, 7·1; OMe, 8·9. $C_{20}H_{21}O_3$·OMe requires C, 74·1; H, 7·1; OMe, 9·1%). The 2,4-*dinitrophenylhydrazone* was deposited from ethyl acetate as orange needles, m. p. 250° (decomp.) (Found: N, 10·9. $C_{27}H_{28}N_4O_7$ requires N, 10·8%), and the *oxime* was obtained as needles, m. p. 210°, from aqueous alcohol (Found: N, 4·2. $C_{21}H_{25}NO_4$ requires N, 3·9%).

3-Isopropylidene-5,6,2′-trimethylgris-2′-en-4′-one (X; H for CO_2Me).—By the general method, the acid chloride of β-(3-isopropyl-5,6-dimethyl-2-benzofuryl)propionic acid was condensed with the methoxymagnesio-derivative of t-butyl acetoacetate and the product, heated with toluene-*p*-sulphonic acid in toluene, afforded a crude β-diketone which failed to crystallise after purification from benzene on a silica column. This diketone (2 g.) was mixed with sulphuric acid monohydrate (25 ml.) at 2° and kept for 2 days. Addition of ice gave a gum which was chromatographed on silica from benzene and then crystallised from light petroleum (b. p. 60—80°), to furnish the *5,6,2′-trimethylgrisenone* as prisms (0·1 g.), m. p. 184° (Found: C, 80·5; H, 7·5. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·8%), $\lambda_{max.}$ 234, 259, 318, 331 mμ (log ε 4·51, 4·21, 4·06, 4·08), $\nu_{max.}$ 1672 cm.$^{-1}$. Its 2,4-*dinitrophenylhydrazone* crystallised from ethyl acetate in orange needles, m. p. 268° (Found: N, 11·9. $C_{25}H_{26}N_4O_5$ requires N, 12·1%).

Methyl 3-Isopropylidene-6-methoxy-2′-methyl-4′-oxogris-2′-en-3′-carboxylate (XI).—The acid chloride from β-(3-isopropyl-6-methoxy-2-benzofuryl)propionic acid (5·2 g.) was dissolved in ether (50 ml.) and added to the methoxymagnesio-derivative (6 g.) of methyl acetoacetate suspended in boiling ether (100 ml.). After 2 hr., the mixture was cooled, and dilute acetic acid was added. The organic layer was washed with water, dried ($MgSO_4$), and evaporated to an oil (6 g.) that crystallised from light petroleum (b. p. 40—60°) to give *methyl α-acetyl-δ-(3-isopropyl-6-methoxy-2-benzofuryl)-β-oxovalerate* in prisms (4 g.), m. p. 81°, having a red ferric reaction [Found: C, 66·6; H, 6·6; OMe, 17·2. $C_{15}H_{16}O_4(OMe)_2$ requires C, 66·7; H, 6·7; OMe, 17·2%]. After this dioxo-ester (1·0 g.) had been kept with sulphuric acid monohydrate (10 ml.) at 2° for 2 days, the neutral cyclisation product was isolated in the usual way and when crystallised from methanol afforded the *methyl 6-methoxyoxogrisencarboxylate* in pale yellow parallelepipeds (0·27 g.), m. p. 194°, $\lambda_{max.}$ 230, 262, 312, 324 mμ (log ε 4·31, 4·12, 3·93, 3·92), $\nu_{max.}$ 1742 (ester), 1678 cm.$^{-1}$ (unsaturated C:O) [Found: C, 70·1; H, 6·6; OMe, 18·0. $C_{18}H_{16}O_3(OMe)_2$ requires C, 70·2; H, 6·5; OMe, 18·1%]. The *2,4-dinitrophenylhydrazone* was obtained as orange-red needles, m. p. 214°, from alcohol (Found: N, 10·6. $C_{26}H_{25}N_4O_8$ requires N, 10·8%).

Methyl 3-Ethylidene-4,6,2′-trimethyl-4′-oxocoumaran-2-spiro-1′-cyclopent-2′-ene-3′-carboxylate (I).—Prepared from the methoxymagnesio-derivative of methyl acetoacetate and the acid chloride (Part II) of 3-ethyl-4,6-dimethyl-2-benzofurylacetic acid by the standard sequence, this *spiran* was obtained as slightly yellow prisms, m. p. 92°, from light petroleum (b. p. 40—60°) (Found: C, 73·0; H, 6·5. $C_{19}H_{20}O_4$ requires C, 73·1; H, 6·5%), $\lambda_{max.}$ 229, 260, 269, 310, 321 mμ (log ε 4·49, 4·22, 4·16, 3·91, 3·94), $\nu_{max.}$ 1724 (ester), 1695 cm.$^{-1}$ (unsaturated C:O). The *2,4-dinitrophenylhydrazone* crystallised from ethyl acetate in yellow needles, m. p. 235° (Found: N, 11·5. $C_{25}H_{24}N_4O_7$ requires N, 11·4%).

Attempted Preparations of Methyl 3-Isopropylidene-4,6,2′-trimethyl-4′-oxogris-2′-en-3-carboxylate (XII) *and of Methyl 3-Isopropylidene-4,6,2′-trimethyl-4′-oxobenzofuran-2-spiro-1′-cyclopent-2′-ene-3′-carboxylate* (XIII).—(i) β-(3-Isopropyl-4,6-dimethyl-2-benzofuryl)propionic acid was converted into the acid chloride and condensed with the methoxymagnesio-derivative of methyl acetoacetate as described for the analogues above. The resulting dioxo-ester formed a yellow oil with an intense ferric reaction but did not crystallise. Attempts to cyclise this ester to a grisen by sulphuric acid by the standard procedure failed to yield any neutral material or to affect the infrared spectrum appreciably. (ii) Taken through the sequence adumbrated in (i), 3-isopropyl-4,6-dimethyl-2-benzofurylacetic acid also failed to yield any neutral spiran. The use of other dehydrating agents and of higher temperatures (60°) led to no different result.

2,3,4,4a,6,6a-Hexahydro-6aα-hydroxy-4aβ,6β,7,9-tetramethyl-3-oxo-1H-5,11-dioxadibenzo[a,d]*pentalene* (IX—XIV).—The dark crystalline complex which separated during 2 days from a solution of 3-ethylidene-4,6,2′-trimethylgris-2′-en-4′-one (1·0 g.) in ether (50 ml.) containing osmium tetroxide (1 g.) and pyridine (2 ml.) was collected, washed with ether, and dried in air. When reduced by a stream of sulphur dioxide, the complex in 80% alcohol (120 ml.) containing charcoal (2 g.) was decomposed after about 40 min. and the mixture was then filtered. The filtrate, when concentrated under reduced pressure and diluted with water, gave a solid which was isolated with ether and crystallised from aqueous alcohol, affording the *4aβ,6β,7,9-tetramethyl-5,11-dioxapentalene* in diamond-shaped plates (0·53 g.), m. p. 151°, $\lambda_{max.}$ 286 mμ (log ε 3·48), with a negative ferric reaction and insoluble in 2N-sodium hydroxide but giving a red Zimmermann reaction (Found: C, 71·5; H, 7·6. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3%). The *2,4-dinitrophenylhydrazone* crystallised from ethyl acetate–methanol in yellow needles, m. p. 221° (Found: C, 59·8; H, 5·3; N, 11·5. $C_{24}H_{26}O_7N_4$ requires C, 59·7; H, 5·4; N, 11·6%).

2,3,4,4a,6,6a-Hexahydro-6aα-methoxy-4aβ,6β,7,9-tetramethyl-3-oxo-1H-5,11-dioxadibenzo[a,d]*pentalene* (XIV; OMe for OH).—The foregoing hydroxy-ketone (0·30 g.) in dimethylformamide (9 ml.) was shaken for 73 hr. with silver oxide (0·9 g.) and methyl iodide (6 ml.). The residues from filtration were washed with small quantities of (1 : 1) ether–dimethylformamide; these washings were combined with the filtrate which was then diluted with ether (60 ml.) and extracted with aqueous potassium cyanide to remove silver salts. After being washed with water and dried (Na_2SO_4), the ethereal solution was evaporated to an oil which, crystallised from methanol, afforded the 6aα-methoxy-5,11-dioxapentalene in prisms (0·10 g.), m. p. 128°. This compound was identified with the product (IV; H for CO_2Me) of ozonolysis of 3-ethylidene-4,6,2′-trimethylgris-2′-en-4′-one (III; H for CO_2Me) by spectroscopic and mixed-melting-point

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methods: specimens from the two preparations also gave the same 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 211°.

**2,3,4,4*a*,6,6*a*-*Hexahydro*-6a*α*-*hydroxy*-4*a*β,6*α*,7,9-*tetramethyl*-3-*oxo*-1H-5,11-*dioxadibenzo*[a,d]-*pentalene* (XV).—The above 6a*α*-hydroxy-4a*β*,6*β*,7,9-tetramethyldioxapentalene (200 mg.) was heated under reflux for 1 hr. with methanol (20 ml.) and N-sodium hydroxide (20 ml.). The cooled solution was diluted with water and extracted with ether (4 × 50 ml.): the extract, washed with water, dried (Na_2SO_4), and evaporated, afforded a solid. This solid supplied the 6a*α*-*hydroxy*-4a*β*,6*α*,7,9-*tetramethyldioxapentalene* as prisms (153 mg.), m. p. 178°, from aqueous alcohol (Found: C, 71·5; H, 7·4%). This compound had $\lambda_{max.}$ 280, 289 mμ (log ε 3·40, 3·44) and $\nu_{max.}$ 3440 cm.$^{-1}$ (OH) and 1705 cm.$^{-1}$ (C:O), gave a negative ferric reaction but a red Zimmermann reaction, and was converted into the 2,4-*dinitrophenylhydrazone* which crystallised from alcohol–ethyl acetate in golden needles, m. p. 268° (decomp.) (Found: C, 59·7; H, 5·4; N, 11·4. $C_{24}H_{26}N_4O_7$ requires C, 59·7; H, 5·4; N, 11·6%).

Methylated by silver oxide and methyl iodide in dimethylformamide in the same way as the isomer above, this alcohol gave **2,3,4,4*a*,6,6*a*-*hexahydro*-6a*α*-*methoxy*-4a*β*,6*α*,7,9-*tetramethyl*-3-*oxo*-1H-5,11-*dioxadibenzo*[a,d]*pentalene* (XV; OMe for OH) as needles, m. p. 159°, from aqueous methanol (Found: C, 72·4; H, 7·9. $C_{19}H_{24}O_4$ requires C, 72·1; H, 7·7%), $\lambda_{max.}$ 1715 cm.$^{-1}$ (C:O), and formed a 2,4-*dinitrophenylhydrazone* crystallising from alcohol–ethyl acetate in yellow needles, m. p. 224° (Found: N, 10·9; OMe, 6·2. $C_{24}H_{25}N_4O_6$·OMe requires N, 11·3; OMe, 6·2%).

**2,3,4,4*a*,6,6*a*-*Hexahydro*-6a*α*-*hydroxy*-4a*β*,7,9-*trimethyl*-3-*oxo*-1H-5,11-*dioxadibenzo*[a,d]*pentalene* (XXI).—Interaction of osmium tetroxide (1 g.), pyridine (1 ml.), and 4,6,2′-trimethyl-3-methylenegris-2′-en-4′-one (1·0 g.) in ether (200 ml.) furnished a dark crystalline complex which was decomposed as described above. The product was an oil that crystallised on addition of a little methanol and could then be purified from aqueous methanol, giving the 6a*α*-hydroxy-4a*β*,7,9-*trimethyldioxapentalene* in needles (0·41 g.), m. p. 141°, $\nu_{max.}$ 3440 (OH), 1724 cm.$^{-1}$ (C:O) (Found: C, 70·2; H, 7·0. $C_{17}H_{20}O_4$ requires C, 70·8; H, 7·0%). Kuhn–Roth estimations gave values of 13·9 (theor. for three *C*-Me groups, 15·0%). The semicarbazone separated from aqueous methanol in plates, m. p. 224° (Found: C, 62·2; H, 6·9; N, 11·5. $C_{18}H_{23}N_3O_4$ requires C, 62·6; H, 6·7; N, 12·2%).

This alcohol was unaffected by boiling 2N-aqueous-alcoholic sodium hydroxide after 1 hr., or by similar treatment with 4N-methanolic sodium methoxide.

**2,3,4,4*a*,6,6*a*-*Hexahydro*-6a*α*-*hydroxy*-9-*methoxy*-4a*β*,6,6-*trimethyl*-3-*oxo*-1H-5,11-*dioxadibenzo*[a,d]*pentalene* (XX).—When the adduct from osmium tetroxide (0·5 g.), pyridine (1 ml.), and 3-isopropylidene-6-methoxy-2′-methylgris-2′-en-4′-one (0·50 g.) was decomposed by sulphur dioxide in the usual way, there resulted a viscous oil which crystallised from ether–light petroleum (b. p. 40—60°) to give the 9-*methoxy*-4a*β*,6,6-*trimethyldioxapentalene* in tiny needles (0·31 g.), m. p. 163°, $\lambda_{max.}$ 284, 290 mμ (log ε 3·68, 3·61), $\nu_{max.}$ 3333 (OH), 1689 cm.$^{-1}$ (C:O) (Found: C, 67·9; H, 7·0; OMe, 9·7. $C_{17}H_{19}O_4$·OMe requires C, 67·9; H, 7·0; OMe, 9·7%). The 2,4-*dinitrophenylhydrazone* separated from ethyl acetate in orange needles, m. p. 208°, $\lambda_{max.}$ 361 mμ (log ε 4·41) (Found: N, 11·0. $C_{24}H_{26}N_4O_8$ requires N, 11·2%).

This alcohol (100 mg.) was recovered after being heated with alcohol (10 ml.) and 2N-sodium hydroxide (4 ml.) for 1 hr.

Ethyl **2,3,4,4*a*,6,6*a*-*Hexahydro*-6a*α*-*hydroxy*-4a*β*,6*β*,7,9-*tetramethyl*-3-*oxo*-1H-5,11-*dioxadibenzo*[a,d]*pentalene*-4-*carboxylate** (VII; CO_2Et for CO_2Me).—Osmium tetroxide (0·5 g.) in ether (40 ml.) containing pyridine (1 ml.) was added to ethyl 3-ethylidene-4,6,2′-trimethyl-4′-oxogris-2′-en-3′-carboxylate (0·65 g.) (Part II), also in ether (100 ml.); precipitation of the brown complex, if not complete in 2 days, was promoted by addition of light petroleum. The *adduct* formed chocolate-coloured needles (1·2 g.), m. p. ~187° (decomp.), from pyridine–light petroleum (Found: * H, 4·7; N, 3·8. $C_{21}H_{24}O_5Os,2C_5H_5N$ requires H, 4·5; N, 3·7%). This adduct had $\nu_{max.}$ 1737 (ester) and 1675 cm.$^{-1}$ (αβ-unsaturated C:O).

The adduct (1·2 g.) in 80% alcohol (120 ml.) containing charcoal (2·0 g.) was reduced by a stream of sulphur dioxide as described for the analogues above; it furnished a gum which crystallised when alcohol was added. The same product resulted when the adduct was reduced by hydrogen sulphide instead of sulphur dioxide; also when the adduct (0·4 g.) in 95% alcohol (75 ml.) was shaken with hydrogen in the presence of 5% palladium–charcoal (1·0 g.) for 1·5 hr., the mixture filtered, the filtrate concentrated, diluted with water, and extracted with ether, and

* Facilities for the determination of carbon in the presence of osmium were not available.

the extract concentrated to a gum (0·13 g.) which solidified when kept. Recrystallised from aqueous alcohol, these solids afforded the ethyl 6aα-hydroxy-4aβ,6β,7,9-tetramethyldioxapentalene as the *ethanol solvate* in thick needles, m. p. 106° (Found: C, 65·6; H, 7·7; OEt, 20·7. $C_{19}H_{21}O_5$·OEt,EtOH requires C, 65·7; H, 7·7; OEt, 21·4%), $\lambda_{max.}$ (in neutral alcohol) 229, 251, and 290 mμ (log ε 4·04, 3·98, 3·52), $\lambda_{max.}$ (in alkaline alcohol) 243 and 280 mμ (log ε 3·40, 4·12), $\nu_{max.}$ 3420, 3290 (OH) and 1641 cm.$^{-1}$ (bonded C:O). The alcohol of crystallisation could be removed efficiently only at 120°, giving a melt (Found: OMe, 12·8%) having infrared absorption bands at 1748 (ester) and 1720 cm.$^{-1}$ (ketone) in addition to those shown by the solvate. This melt could not be crystallised except from alcohol, in which the solvate was regenerated, or from methanol, which gave material containing variable amounts of methanol of crystallisation and having properties closely similar to those of the ethanol solvate.

The ethanol solvate behaved as a β-oxo-ester in giving a red ferric reaction but a negative Zimmermann reaction and in dissolving in dilute alkali. It afforded *ethyl 6aα-hydroxy-3-hydroxyimino-4aβ,6β,7,9-tetramethyl-5,11-dioxapentalene-4-carboxylate* which separated from aqueous alcohol in needles, m. p. 220° (decomp.), $\nu_{max.}$ 3450, 3370 (OH), 1724 cm.$^{-1}$ (ester) (Found: C, 64·9; H, 6·9; N, 3·7; OEt, 11·2. $C_{19}H_{22}NO_5$·OEt requires C, 64·8; H, 7·0; N, 3·6; OEt, 11·6%).

Methyl 2,3,4,4a,6,6a-Hexahydro-6aα-hydroxy-4aβ,6β,7,9-tetramethyl-3-oxo-1H-5,11-dioxadibenzo[a,d]*pentalene-4-carboxylate* (VII).—Prepared in the same way as the ethyl ester above from the appropriate grisenone (0·6 g.), this methyl ester crystallised from methanol as the *methanol solvate*, needles (0·4 g.), m. p. 148°, $\nu_{max.}$ 3460 (OH), 1630 cm.$^{-1}$ (bonded C:O) (Found: C, 63·8; H, 7·5; OMe, 12·7. $C_{19}H_{21}O_5$·OMe,MeOH requires C, 64·3; H, 7·2; OMe, 15·8%). When ethanol replaced methanol in these reactions, the product was the *ethanol solvate*, needles, m. p. 147° (not depressed on admixture with the methanol solvate) (Found: C, 64·8; H, 7·4; alkoxyl as OMe, 9·2. $C_{19}H_{21}O_5$·OMe,EtOH requires C, 65·0; H, 7·4; alkoxyl as OMe, 15·3%). Both solvates were soluble in dilute alkali and gave red ferric reactions. Kept *in vacuo* at 120°, the methanol solvate did not lose its crystalline habit but eventually afforded the solvent-free *methyl dioxapentalene-4-carboxylate* (Found: C, 66·8; H, 6·8; OMe, 8·0. $C_{19}H_{21}O_5$·OMe requires C, 66·7; H, 6·7; OMe, 8·6%). This solid had almost the same infrared absorption spectrum as the solvates, but when it had been melted a band at 1723 cm.$^{-1}$ (ester) developed.

The two solvates gave the same (solvent-free) *oxime*, which crystallised from aqueous alcohol in needles, m. p. 221°, $\nu_{max.}$ 3495, 3320 (OH), 1727 cm.$^{-1}$ (ester) (Found: C, 64·2; H, 6·7; N, 3·7; OMe, 8·1. $C_{19}H_{22}NO_5$·OMe requires C, 64·0; H, 6·7; N, 3·7; OMe, 8·3%).

4-Acetyl-2,3,4,4a,6,6a-hexahydro-6aα-hydroxy-4aβ,6β,7,9-tetramethyl-3-oxo-1H-5,11-dioxadibenzo[a,d]*pentalene* (XVI).—The adduct which separated from a solution of osmium tetroxide (1 g.), pyridine (2 ml.), and 2′-acetyl-3-ethylidene-4,6,2′-trimethylgris-2′-en-4′-one (1·24 g.) (Part II) in ether (200 ml.) was reduced by sulphur dioxide in 20% aqueous methanol. Recovered in the usual way, the oily product eventually solidified and crystallised from aqueous alcohols with varying amounts of alcohols of crystallisation. Crystallised from benzene–light petroleum (b. p. 60—80°), however, these solvates furnished the *4-acetyl-6aα-hydroxy-4aβ,6β,7,9-tetramethyldioxapentalene* in needles (0·80 g.), m. p. 164°, with a red ferric reaction (Found: C, 69·5; H, 7·0. $C_{20}H_{24}O_5$ requires C, 69·8; H, 7·0%). This ketone had $\nu_{max.}$ 3401 (OH), 1695 and 1672 (both weak; C:O), and 1577 (strong; bonded C:O).

Ethyl 1,2,3,3a,5,5a-Hexahydro-5aα-hydroxy-3aβ,6,8-trimethyl-2-oxo-4,10-dioxabenzo[a]*cyclopenta*[d]*pentalene-3-carboxylate*.—When oxidised by osmium tetroxide as in the examples above, ethyl 3-methylene-4,6,2′-trimethyl-4′-oxocoumaran-2-spiro-1′-cyclopent-2′-ene-3′-carboxylate (0·60 g.) was converted into the *ethyl hydroxytrimethyldioxapentalene-3-carboxylate* which separated from aqueous alcohol in needles or plates (0·38 g.), m. p. 148°, $\lambda_{max.}$ 208, 226, 278, 288 mμ (log ε 4·62, 4·13, 3·48, 3·49), soluble in dilute alkali and having a red ferric reaction (Found: C, 65·5; H, 6·5; OEt, 11·3. $C_{17}H_{17}O_5$·OEt requires C, 65·9; H, 6·4; OEt, 13·0%). This compound had, in the crystalline state, $\nu_{max.}$ 3440 (OH) and 1650 cm.$^{-1}$ (bonded C:O), and in the fused state 3440 (OH) and 1727 cm.$^{-1}$ (ester).

The *oxime* crystallised from benzene–methanol in needles, m. p. 200° (decomp.), $\nu_{max.}$ 1736 cm.$^{-1}$ (ester) (Found: N, 3·6. $C_{19}H_{23}NO_6$ requires N, 3·9%).

Methyl 1,2,3,3a,5,5a-Hexahydro-5aα-hydroxy-3aβ,5β,6,8-tetramethyl-2-oxo-4,10-dioxabenzo[a]*cyclopenta*[d]*pentalene-3-carboxylate* (VI).—By the method used in the foregoing example, methyl 3-ethylidene-4,6,2′-trimethyl-4′-oxocoumaran-2-spiro-1′-cyclopent-2′-ene-3′-carboxylate (0·6 g.) was oxidised to the *methyl hydroxytetramethyldioxapentalenecarboxylate* which, when purified

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from methanol, formed needles or plates (0·3 g.), m. p. 152—154°, $\lambda_{max.}$ 212, 229, 280, 290 mμ (log ε 4·42, 4·12, 3·46, 3·48), $\nu_{max.}$ 3704 (OH), 1660 cm.$^{-1}$ (bonded C:O) (Found: C, 65·9; H, 6·6; OMe, 9·0. $C_{18}H_{19}O_5$·OMe requires C, 65·9; H, 6·4; OMe, 9·0%).

3aα-2′-Carboxyethyl-3α-carboxymethyl-1,3,3a,8b-tetrahydro-8bα-hydroxy-1,3β,6,8-tetramethyl-2,4-dioxacyclopenta[a]*indene* (XVII; R = OH).—The ethyl hydroxy-4aβ,6β,7,9-tetramethyldioxapentalenecarboxylate (VII) (1·0 g.) was heated under reflux with 2N-sodium hydroxide for ¾ hr. Insoluble material which had been formed was isolated with ether and crystallised from alcohol–light petroleum (b. p. 60—80°), giving the 4αβ,6α,7,9-tetramethyldioxapentalene (IX) in prisms (0·12 g.), m. p. and mixed m. p. 177°, and thence the 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 268°. On acidification, the alkaline solution deposited a solid. This was collected into ether, washed with water, dried (Na_2SO_4), recovered by evaporation of the solvent, and purified from aqueous alcohol, giving the *3aα-2′-carboxyethyl-3α-carboxymethyldioxacyclopenta*[a]*indene* (XVII; R = OH) in hexagonal prisms (0·30 g.), m. p. 224° (decomp.), pK_a (potentiometric titration in water) 4·75 (one inflection) [Found: C, 62·5; H, 6·6%; equiv., 187. $C_{17}H_{22}O_5(CO_2H)_2$ requires C, 62·6; H, 6·6%; equiv., 182]. This acid gave negative results in tests with ferric chloride, sodium nitroprusside, Ehrlich's reagent, and Zimmermann's reagent. With diazomethane, it afforded the *dimethyl ester* crystallising from methanol and then light petroleum (b. p. 40—60°) in needles, m. p. 112°, $\nu_{max.}$ (in $CHCl_3$) 3410 (OH), 1733 cm.$^{-1}$ (ester), $\nu_{max.}$ (in Nujol) 3470, 1736, 1721 cm.$^{-1}$, $\lambda_{max.}$ 280, 286 mμ (log ε 3·42, 3·45) [Found: C, 64·4; H, 7·1; OMe, 15·6. $C_{19}H_{22}O_5(OMe)_2$ requires C, 64·3; H, 7·1; OMe, 15·8%].

When this diacid was kept at its m. p. until effervescence ceased, a glass was formed which, when crystallised from benzene, afforded a *lactone* in plates, m. p. 187°, $\nu_{max.}$ 1754, (δ-lactone), 1721 cm.$^{-1}$ (CO_2H) [Found: C, 65·5; H, 6·5%; equiv. (direct titration) 342, (back-titration) 173. $C_{18}H_{21}O_4$·CO_2H requires C, 65·9; H, 6·4%; equiv., 346].

Lactone (XVIII) *of 3α-Acetonyl-3aα-2′-carboxyethyl-1,3,3a,8b-tetrahydro-8bα-hydroxy-1,3β,6,8-tetramethyl-2,4-dioxacyclopenta*[a]*indene* (XVII; R = Me).—The 4-acetyl-6α-hydroxy-4aβ,6β,7,9-tetramethyldioxapentalene (XVI) (0·5 g.), when heated under reflux for 1 hr. with 2·5N-sodium hydroxide, gave a neutral and an acidic product. The former crystallised from light petroleum (b. p. 60—80°), giving the hydroxy-4aβ,6α,7,9-tetramethyldioxapentalene (IX) in plates, m. p. and mixed m. p. 177°, further identified spectroscopically. The latter formed a brownish oil which could not be satisfactorily purified. Slow distillation at 140°/0·1 mm. afforded the *lactone* as a glass, $\nu_{max.}$ 1761 (δ-lactone) and 1706 cm.$^{-1}$ (C:O) (no OH absorption) (Found: C, 69·5; H, 7·0. $C_{20}H_{24}O_5$ requires C, 69·8; H, 7·0%).

γ-Lactone (XIX) *of 3α,3aα-Biscarboxymethyl-1,3,3a,8b-tetrahydro-8bα-hydroxy-1,3β,6,8-tetramethyl-2,4-dioxacyclopenta*[a]*indene.*—The methyl 5aα-hydroxytetramethyldioxapentalenecarboxylate (VI) (1 g.) was heated under reflux in an atmosphere of nitrogen for 4 hr. with 10% aqueous potassium hydroxide (25 ml.). The cooled solution was acidified with concentrated hydrochloric acid, and the organic materials were isolated by repeated extraction with benzene. These extracts were dried ($MgSO_4$) and concentrated: the residue was taken up in 1 : 1 benzene–light petroleum and left. After 15 days, prisms had separated. A second crop was garnered after a further 8 days. A week later, a third crop had separated. The first two crops were recrystallised in a similar fashion, giving the *γ-lactone* in prisms (0·3 g.), m. p. 170°, $\lambda_{max.}$ 212, 280, 287 mμ (log ε 4·11, 3·36, 3·39), $\nu_{max.}$ 1779 (γ-lactone), 1695 cm.$^{-1}$ (CO_2H) [Found: C, 64·9; H, 6·1%; equiv. (direct titration) 335, (back-titration) 155. $C_{17}H_{19}O_4$·CO_2H requires C, 65·1; H, 6·1%; equiv., 332]. The third crop had infrared absorption consistent with the presence of this lactonic acid together with the parent hydroxy-diacid: when heated, it afforded further quantities of the pure lactone.

With diazomethane in ether, the lactonic acid furnished the *methyl ester* separating from benzene in cubes, m. p. 130° (Found: C, 65·9; H, 6·5; OMe, 9·2. $C_{18}H_{19}O_5$·OMe requires C, 65·9; H, 6·4; OMe, 9·0%), $\lambda_{max.}$ 286 mμ (log ε 3·49), $\nu_{max.}$ 1786 (γ-lactone) and 1738 cm.$^{-1}$ (ester).

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UNIVERSITY OF LIVERPOOL. [*Received, May 4th,* 1960.]

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60. *Peroxides of Elements other than Carbon. Part VII.*[1] *The Relative Reactivity of the t-Butyl and the Isobutyl Group in the Autoxidation of Di-isobutyl-t-butylboron.*

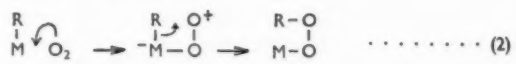
By Alwyn G. Davies, D. G. Hare, and R. F. M. White.

The same order of reactivity of the alkyl groups, $Bu^t > Bu^i$, holds in the reaction of di-isobutyl-t-butylboron with hydrogen peroxide and with molecular oxygen. It is believed from other evidence that the former reaction involves a nucleophilic 1,2-rearrangement of an alkyl group from boron to oxygen, and it is suggested that these results are compatible with a mechanism for the reaction with oxygen involving now a nucleophilic 1,3-rearrangement from boron to oxygen.

The autoxidation of an organometallic compound gives initially an organoperoxymetallic compound:

$$MR + O_2 \longrightarrow MO{\cdot}OR \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$
$$(M = Li,[2,3]\ Mg,[3,4]\ Zn,[3,4,5]\ Cd,[3,6]\ B,[3,7]\ Al,[2,8])$$

From the change in reactivity as the organometallic compound was varied, and as other reagents were added, it was suggested that the reaction involved nucleophilic attack of oxygen upon the metal, accompanied or followed by a nucleophilic 1,3-rearrangement of the alkyl group from the metal to oxygen:[3,7b]



$\ldots\ldots\ldots$ (2)

Further evidence has now been obtained by partial autoxidation of a mixed alkyl, MRR′, and analysis of the product for RM·O·OR′ and R′M·O·OR; the above mechanism might be expected to involve a similar order of relative mobility of the groups R and R′ as in the oxidation of the same mixed alkyl with hydrogen peroxide, which involves a nucleophilic 1,2-rearrangement:[7b,d,9,10]

$\cdots\cdots$ (3)

The choice of a compound for study is severely limited. Arylmetallic compounds cannot be used because the arylperoxy-structure is not stable, and the only known autoxidisable mixed alkylmetallic compounds that do not disproportionate are those of zinc or the very few of boron which contain a tertiary alkyl group. We have therefore used di-isobutyl-t-butylboron because it has been fully characterised[7b,11] and because we had had experience in the autoxidation of boron alkyls.[7b,c,d]

The possible products from the hydrogen peroxide oxidations would be $R_2B{\cdot}OH$ + ROH, and then $R{\cdot}B(OH)_2$ + 2ROH; from the autoxidation one would expect $R_2B{\cdot}O{\cdot}OR$

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[4] Walling and Buckler, *J. Amer. Chem. Soc.*, 1953, **75**, 4372.
[5] Abraham, *Chem. and Ind.*, 1959, 750.
[6] Davies and Packer, *Chem. and Ind.*, 1958, 1177; *J.*, 1959, 3164.
[7] (*a*) Petry and Verhoek, *J. Amer. Chem. Soc.*, 1956, **78**, 6416; (*b*) Abraham and Davies, *Chem. and Ind.*, 1957, 1622; *J.*, 1959, 429; (*c*) Davies and Hare, *J.*, 1959, 438; (*d*) Davies, Hare, and White, *Chem. and Ind.*, 1959, 1315; *J.*, 1960, 1040.
[8] Hall, Thesis, London, 1959; Davies and Hall, unpublished work.
[9] Kuivila and his co-workers, *J. Amer. Chem. Soc.*, 1957, **79**, 5659 and earlier papers.
[10] Davies and Moodie, *J.*, 1958, 2372.
[11] Hennion, McCusker, Ashby, and Rutkowski, *J. Amer. Chem. Soc.*, 1957, **79**, 5190; Hennion, McCusker, and Rutkowski, *ibid.*, 1958, **80**, 617.

and then $R{\cdot}B(O{\cdot}OR)_2$. In the products of any one oxidation the three groups R would be composed of t-butyl and isobutyl groups in the ratio of 1 : 2, and it was necessary to determine the location of these groups. This has been done principally by vapour-phase chromatography of the fragments of oxidation by peroxyacid,[7b,c,d,12] by determining the proton magnetic resonance spectra of the organoboron compounds,[7d] and, where suitable, by isolating characteristic solid derivatives. These methods gave concordant results.

Oxidation with Hydrogen Peroxide.—Di-isobutyl-t-butylboron was treated with hydrogen peroxide (1 mol.) in ether, giving as the only products t-butyl alcohol (identified chromatographically) and isobutylboronous acid (identified by m. p. and by the proton magnetic resonance and infrared spectra of the anhydride). Therefore in the rearrangement generalised in equation (3), the t-butyl group migrates from boron to oxygen to the exclusion of the isobutyl group.

This order is reasonable in the light of our knowledge of the nucleophilic migration of alkyl groups from carbon to oxygen in the Baeyer–Villiger oxidation of ketones with peroxyacids. Although no experiments with isobutyl t-butyl ketone have been reported, it appears that in general t-alkyl groups are more mobile than primary alkyl groups. For example, in the oxidation of ketones, Ph·COR, with trifluoroperoxyacetic acid,[13] the mobilities of groups R compared with phenyl are: Et 7×10^{-2}; Pr^n 7×10^{-2}; neopentyl $1{\cdot}1 \times 10^{-1}$; and Bu^t 39; *i.e.*, $Bu^t : R^p = 550—350 : 1$.

Oxidation with Molecular Oxygen.—It was first shown that di-isobutyl-t-butylboron in dilute solution, like the other tributylborons which we have investigated,[7b,c,d] will absorb 2 mol. of oxygen to give a diperoxide, $Bu{\cdot}B(O{\cdot}OBu)_2$. The reaction is exothermic and the first mol. of oxygen is taken up about twice as fast as the second. The oxidation is slowed by benzylamine and inhibited completely by a 100-fold molar excess.

Di-isobutyl-t-butylboron in ether was then allowed to absorb varying amounts of oxygen; peroxyoctanoic acid was immediately added to convert, after hydrolysis, alkyl groups into the corresponding alcohols and alkylperoxy-groups into the corresponding alkyl hydroperoxides:[7b]

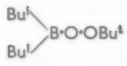
$$R_n{\cdot}B(O{\cdot}OR')_{3-n} + n\mathbf{C}_7H_{15}{\cdot}CO_3H \xrightarrow{H_2O} n\mathrm{ROH} + (3-n)R'O{\cdot}OH + B(OH)_3 \quad . \quad . \quad . \quad . \quad (4)$$

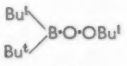
The mixture of iso- and t-butyl alcohol and hydroperoxides was then quantitatively analysed by vapour-phase chromatography. The results are shown in Table 1.

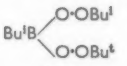
TABLE 1. *Products of partial autoxidation of di-isobutyl-t-butylboron.*

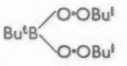
O_2 absd. (mol.)	Bu^tO_2H (mol.)	Bu^iO_2H (mol.)	Bu^tOH (mol.)	Bu^iOH (mol.)	$\Sigma Bu^i/\Sigma Bu^t$ (mol.)
0·00	0·00	0·00	1·00	2·00	2·00
0·36	0·25	0·11	0·75	1·89	2·00
1·08	0·75	0·33	0·28	1·64	1·91
1·10	0·75	0·35	0·27	1·63	1·94
1·98	0·99	0·99	0·02	1·01	1·98

During the uptake of the first mol. of oxygen the relative mobilities of the t-butyl and isobutyl groups are about 4·5 : 1, giving a product equivalent to 69% of compound (I) and 31% of compound (II). The selectivity during the uptake of the second mol. of oxygen is some ten times as great, and the ultimate product consists of about 99% of compound (III) and 1% of compound (IV).


(I)


(II)

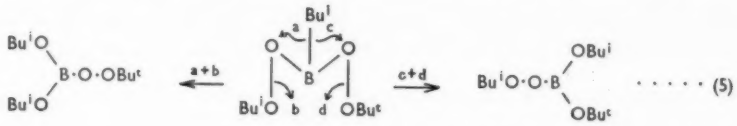

(III)


(IV)

The ether was rapidly removed from a solution which had absorbed 2 mol. of oxygen, giving essentially pure isobutyl-isobutylperoxy-t-butylperoxyboron (III) as a colourless

[12] Abraham, Davies, Llewellyn, and Thain, *Analyt. Chim. Acta*, 1957, **17**, 499.
[13] Hawthorne, Emmons, and McCallum, *J. Amer. Chem. Soc.*, 1958, **80**, 6393.

oil. The proton magnetic resonance spectrum of freshly prepared material, shown in the Figure (*a*), is compatible with this structure. At room temperature the doublet of the methyleneoxy-group and the singlet of the t-butoxy-group rapidly developed. We believe that this decomposition proceeds by the redox rearrangement of the peroxide (reaction 5); the relative size of the peaks then indicates that, as might be expected on



. . . . . (5)

the basis of this mechanism, the isobutylperoxy-group is reduced (shifts a and b) more readily than the t-butylperoxy-group (shifts c and d).

A similar rearrangement is probably involved in the reduction which accompanies the hydrolysis of the peroxide.[7b] Chromatography of the alcohols and hydroperoxides which are formed showed that the isobutylperoxy-group is again reduced more readily (by a factor of about 5) than the t-butylperoxy-group.

The same order of reactivity, Bu^t > Bu^i, therefore holds in the reaction of di-isobutyl-t-butylboron with hydrogen peroxide and with oxygen. The mechanism of the first reaction is reasonably well established as nucleophilic 1,2-rearrangement of alkyl from boron to oxygen (reaction 3).* These results therefore appear compatible with the mechanism proposed for the autoxidation reactions, involving a nucleophilic 1,3-rearrangement from boron to oxygen (reaction 2).

Autoxidation of the pure boron alkyl to a boronic ester, Bu·B(OBu)$_2$, involves successively both these types of rearrangement, in both of which the Bu^{t}B group is the more reactive. As expected, the proton magnetic resonance spectrum of the product [Fig. (*c*)] showed it to have the structure Bu^i·B(OBu^t)·OBu^i; hydrolysis gave isobutylboronic acid, m. p. 112°, identified by the proton magnetic resonance spectrum of its anhydride and by the preparation of its crystalline diethanolamine ester.†

Two further experiments were carried out. First, we tried to confirm the composition of the product after only one mol. of oxygen was absorbed by the boron alkyl in carbon tetrachloride. The proton magnetic resonance of the solution, however, showed that the product was the compound Bu^{i}B(OBu^t)(OBu^i), and t-butyl chloride and carbonyl chloride were detected. These products could be accounted for if it were supposed that the autoxidation of the boron alkyl induces oxidation of the carbon tetrachloride to carbonyl chloride and chlorine, and that the chlorine (cf. hydrogen peroxide, above) reacts preferentially with the Bu^{t}B group to give t-butyl chloride. An analogous situation is encountered in the autoxidation of benzaldehyde in carbon tetrachloride, where carbonyl chloride is also formed.[17] A solution of the pure diperoxide, R·B(O·OR)$_2$, in carbon tetrachloride also liberated carbonyl chloride but apparently somewhat more slowly than it was formed during the above autoxidation. This might be taken to indicate, contrary to our conclusions above, that the autoxidation of the boron alkyl follows a homolytic mechanism.

Secondly, an attempt was made to see if the autoxidation would initiate polymerisation

* We have shown [14] that, as this mechanism requires, neopentylboron compounds are oxidised to neopentyl alcohol and no t-pentyl alcohol is formed.

† This confirms the view that the boronic acid, m. p. 113°, which Krause and Nobbe [15] obtained by the autoxidation of what was then thought to be tri-t-butylboron, was in fact isobutyl- rather than t-butyl-boronic acid.[16]

[14] Hare, Thesis, London, 1960.
[15] Krause and Nobbe, *Ber.*, 1931, **64**, 2112.
[16] See ref. 7*b*, p. 431.
[17] Jorissen and van der Beek, *Rec. Trav. chim.*, 1927, **46**, 44.

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of an olefin. Acrylonitrile which is stable towards boron alkyls under nitrogen,[18] is polymerised rapidly if oxygen is admitted, but is equally rapidly polymerised in the presence of di(isobutylperoxy)isobutylboron (Table 3). This experiment is thus inconclusive as to the mechanism of the autoxidation. It seems reasonable to suggest that the peroxide, $R{\cdot}B(O{\cdot}OR)_2$, and the monomer form a complex[19] which undergoes O–O homolysis and induces polymerisation.[20] The situation differs, however, from that described by Bawn, Margerison, and Richardson[20] for polymerisation of methyl methacrylate in that no molecule of trialkylboron is involved.

Experimental

The interconversion of the esters, acids, and anhydrides of boronous and boronic acids, and the determination and interpretation of the proton magnetic resonance spectra, have been described previously.[7d] Vapour-phase chromatography was carried out by comparison with standard mixtures through a column usually of glycerol on "Celite" at $\geqslant 80°$.[12] This gives better separation of alcohols and hydroperoxides than does dinonyl phthalate. The use of a fire-brick support is not recommended because it can induce decomposition of the hydroperoxides, perhaps because of the presence of metal ions such as Fe^{2+}.

Di-isobutyl-t-butylboron.—Di-isobutyl-t-butylboron, b. p. 49°/2·7 mm., n_D^{25} 1·4240, was prepared by treating the boron trifluoride–ether complex with t-butylmagnesium chloride.[7d] The infrared spectrum was similar to that described in the literature;[11] the structure was checked as follows.

96% Hydrogen peroxide (0·4821 g., 3 mol.) in dry ether (2 c.c.) was added during 1 hr. to a stirred solution of the alkyl (0·7967 g., 1 mol.) in ether (5 c.c.) containing powdered sodium hydroxide at 0°. After a further 4 hr. the mixture was filtered and dried (KOH). The vapour-phase chromatogram (dinonyl phthalate) showed the presence of t-butyl alcohol and isobutyl alcohol in the molar ratio of 1·0 : 2·0. A similar result was obtained by oxidation with peroxyoctanoic acid (see below).

Autoxidation of Di-isobutyl-t-butylboron.—Autoxidations were carried out at the gas-burette as described previously;[7b] the results are given in Table 2.

Table 2. *Autoxidation of di-isobutyl-t-butylboron.*

Solvent	Volume (c.c.)	R_3B (g.)	Time (min.)	O_2 absd. (mol.)	Peroxide formed [a] (mol.)
Et_2O	70	0·3325	60	1·90	1·88
Et_2O	200	0·8204	180	*b*	1·94
$MeNO_2$	50	0·3273	120	1·96	1·84
C_6H_6	50	0·3200	90	1·85	1·69
PhOMe	50	0·3247	90	1·89	1·75

[a] Determined iodometrically. We now believe that these values are inclined to be low; quantitative hydrogenolysis (see below) gives slightly higher and more accurate values. [b] Oxygen was dispersed through a sintered-glass plate into the solution; the reaction is probably complete in 30 min.

Diethanolamine Esters of Boronic Acids.—The diethanolamine esters are very resistant to hydrolysis and autoxidation and are convenient crystalline derivatives of boronic compounds. They are readily prepared by warming together the boronic compound and diethanolamine, alone or in a solvent. Thus di-n-butyl s-butylboronate and diethanolamine gave the *diethanolamine ester*, m. p. 156° (from acetonitrile) (Found: C, 56·4; H, 10·8. $C_8H_{17}BNO_2$ requires C, 56·2; H, 10·6%) (experiment by Dr. R. B. Moodie).

Di-n-butyl isobutylboronate similarly gave the corresponding *derivative*, needles (from acetonitrile), m. p. 155° (Found: C, 56·0; H, 10·7%), and t-butylboronic anhydride gave the *derivative*, needles (from acetonitrile), m. p. 248° (Found: C, 56·3; H, 10·5%).

Peroxy-acid Oxidation of Alkylperoxyboron Compounds.—The alkyl and alkylperoxy-groups in compounds of the structure $R_n{\cdot}B(O{\cdot}OR)_{3-n}$ were analysed by quantitative oxidation by

[18] Kolesnikov and Klimentova, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1957, 652.
[19] Lyle, DeWitt, and Pattison, *J. Org. Chem.*, 1956, **21**, 61.
[20] Bawn, Margerison, and Richardson, *Proc. Chem. Soc.*, 1959, 397.

reaction (4). The alcohols and hydroperoxides were then determined by vapour-phase chromatography. Peroxyoctanoic acid, which is readily obtained pure,[21] is more convenient than peroxybenzoic acid which we used previously.[7b]

The boron compound (*ca.* 0·2—0·4 g.) in ether (5 c.c.) under nitrogen was treated dropwise with the calculated amount of peroxyoctanoic acid in ether. The mixture was stirred for 1 hr. and the bulk of the ether removed under reduced pressure. (The vapour-phase chromatogram confirmed that no oxidation products were removed at this stage.) Water (3 mol.) was added and the mixture was stirred for 1—3 hr. at room temperature to hydrolyse the borate. All volatile material was then removed into a trap at −75°/1 mm. and analysed chromatographically.

The procedure was checked by the recovery of mixtures of known composition, and by the analysis of di-isobutyl-t-butylboron and of isobutylisobutylperoxy-t-butylperoxyboron, for which there was independent evidence of structure.

Hydrogenolysis of Alkylperoxyboron Compounds.—Although alkylperoxyboron compounds are stable to hydrogen in the presence of Raney nickel, they are readily reduced over platinum oxide at room temperature and pressure; this reduction may take place directly on the boron peroxide, or indirectly on the hydroperoxide formed by hydrolysis by water derived from the platinum oxide. The following procedure was convenient for the hydrogenolysis *in situ* of peroxides formed by autoxidation at the gas-burette.

The burette was filled with hydrogen and a capsule of platinum oxide (0·02—0·04 g./g. of peroxide) under nitrogen was broken under the solvent. The solution was stirred magnetically until the uptake of hydrogen was complete (*ca.* 90 min.). A correction was made for the amount of hydrogen absorbed in the reduction of the platinum oxide.

The method was developed by using di-(s-butylperoxy)-s-butylboron (Found, by hydrogenolysis: peroxidic O, 26·0. Calc. for $C_{12}H_{27}BO_4$: peroxidic O, 26·0%), and yielded crude s-butylboronic acid, m. p. 84—87°.

Partial Oxidation of Di-isobutyl-t-butylboron with Hydrogen Peroxide.—All operations were conducted under nitrogen. A capsule of the boron alkyl (0·8529 g., 1·0 mol.) was broken in dry ether (3·0 c.c.) at 0°. 100% Hydrogen peroxide (0·1595 g., 1·0 mol.) in ether (3·12 c.c.) was added dropwise during 0·75 hr. to the stirred solution. After a further 3 hr. at 0° the clear solution was warmed to room temperature and transferred to one limb of a molecular still of inverted Y design, and degassed.

Material volatile at 0·005 mm. was collected in the second limb at −75°; the vapour-phase chromatogram showed the presence of only t-butyl alcohol (and ether), and the absence of isobutyl alcohol.

The residual white solid showed the presence of a strong infrared band for the HO group. With the receiver at −180° the compound sublimed, giving isobutylboronous acid, m. p. 93—95° with dehydration. This was dehydrated overnight over phosphoric oxide at 18 mm., giving isobutylboronous anhydride as a colourless oil (Found: B, 8·90. Calc. for $C_{16}H_{36}B_2O$: B, 8·15%). The proton magnetic resonance spectrum showed the presence of the isobutyl group and the absence of the t-butyl group. This spectrum, and the infrared spectrum, were identical with those of an authentic sample of isobutylboronous anhydride prepared by treating tri-isobutylboron (1 mol.) with hydrogen peroxide (1 mol.) by the above procedure.

Partial Oxidation of Di-isobutyl-t-butylboron with Oxygen.—A capsule of di-isobutyl-t-butylboron was broken in dry ether (100 c.c.) at the gas-burette and allowed to absorb a precalculated amount of oxygen. (The uptake could be measured only approximately at this stage because the reaction is fast and strongly exothermic, giving a rise in temperature of about 9°, and causing the vapour pressure of the ether to increase during the experiment. An accurate measure of the oxygen absorbed is given by the chromatographic analyses below.) The oxygen in the apparatus was then replaced with nitrogen (through the tap C, Fig. 2 of ref. 7*b*) and the peroxyoctanoic acid in slight excess was added to the stirred solution; these two operations were completed within 1 min. of the end of the autoxidation.

The mixture was stirred for 1 hr. and concentrated at the same time by evaporating most of the ether in a stream of nitrogen (a vapour-phase chromatogram showed that no alcohol or hydroperoxide was lost by this procedure). The product was hydrolysed with water (3 mol.) for 3 hr. All volatile material was collected in a trap at −75°/1 mm., and analysed chromatographically for t- and iso-butyl hydroperoxide and alcohols. No other product was present.

[21] Parker, Ricciuti, Ogg, and Swern, *J. Amer. Chem. Soc.*, 1955, **77**, 4037.

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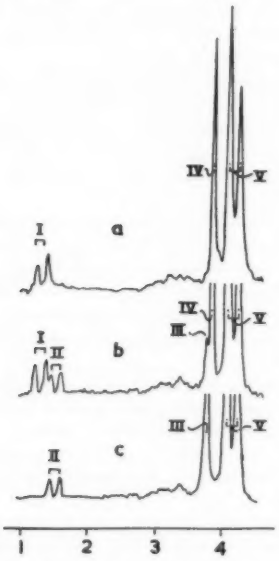
The results are shown in Table 1, where the amount of oxygen absorbed is calculated from the ratio of total hydroperoxides to total alcohols. Some check on the analytical techniques is provided by the molar ratio of total isobutyl compounds to total t-butyl compounds ($\sum Bu^i/\sum Bu^t$) which should be 2 : 1.

Isolation and Identification of Isobutylisobutylperoxy-t-butylperoxyboron.—Isolation. A capsule of di-isobutyl-t-butylboron (0·4824 g.) was broken under dry ether (50 c.c.) through which dry oxygen was passed. After 1·75 hr. the solution was filtered from glass in a dry box,

Proton magnetic resonance spectra.



(*a*) $Bu^iB(O{\cdot}OBu^i)(O{\cdot}OBu^t)$. (*b*) $Bu^iB(O{\cdot}OBu^i)(O{\cdot}OBu^t)$ *partially rearranged to* $Bu^iO{\cdot}O{\cdot}B(OBu^i){\cdot}OBu^t$ *and* $Bu^tO{\cdot}O{\cdot}B(OBu^i)_2$ (reaction 5) *after 1·75 hr. at room temperature.* (*c*) $Bu^iB(OBu^i)(OBu^t)$.

δ values [τ] *are given in the annexed Table.*

Structural assignments of resonances

Fig.	(I) $CH{\cdot}C\mathbf{H}_2{\cdot}O{\cdot}OB$		(II) $CH{\cdot}C\mathbf{H}_2{\cdot}OB$		(III) $(C\mathbf{H}_3)_2C{\cdot}OB$	(IV) $(C\mathbf{H}_3)_3C{\cdot}O{\cdot}OB$	(V) $(C\mathbf{H}_3)_2CH{\cdot}CH_2$	
a	1·18	1·35	—		—	3·83	4·05	4·20
b	1·18	1·35	1·43	1·57	3·78	3·83	4·05	4·20
c	—		1·41	1·55	3·78	—	4·10	4·25

and the ether rapidly removed under reduced pressure, leaving *isobutylisobutylperoxy-t-butylperoxyboron* as a colourless oil [Found: peroxidic O, 21·0 (iodometrically). $C_{12}H_{27}BO_4$ requires Peroxidic O, 26·0%. We now know this method of analysis to give low peroxide values].

Proton magnetic resonance. The proton magnetic resonance spectrum of the product is shown in the Figure (*a*) and shows clearly the presence of Bu^iB, $Bu^iO{\cdot}O$, and $Bu^tO{\cdot}O$ groups (see legend). This spectrum was obtained within 10 min. of the end of the autoxidation; if the operations were conducted more slowly, the spectrum showed that some redox rearrangement had occurred, giving the isobutoxy and t-butoxy groups, as in the Figure (*b*).

Hydrogenolysis. Hydrogenolysis of the peroxide gave isobutylboronic acid as white plates (from water), m. p. 112·5°. It was dehydrated to the anhydride; the proton magnetic resonance spectrum was identical with that of authentic isobutylboronic anhydride, and showed the absence of t-butyl groups.

Hydrolysis. A solution of the peroxide (*ca.* 0·25 g.) in ether (2 c.c.) was shaken with 5N-sodium hydroxide (5 c.c.) for 2 hr. and then extracted with ether. The extract was dried ($MgSO_4$), the bulk of the ether removed, and the product analysed chromatographically. The only compounds present were (molar ratios, out of 3, in parentheses): Bu^tOH (0·158); Bu^iOH (1·80); Bu^tO_2H (0·845); Bu^iO_2H (0·192) (Found: Total peroxide/total alcohol, 0·53; calc., 0·50. Found: total t-butyl compounds/isobutyl compounds, 0·50; calc., 0·50).

Autoxidation of Undiluted Di-isobutyl-t-butylboron.—The boron alkyl (5 g.) in a loosely stoppered bottle was allowed to absorb air slowly during 42 days in a dry box (P_2O_5). The proton magnetic resonance spectrum [Figure (*c*)], showed the product to be isobutyl t-butyl isobutylboronate, $Bu^i{\cdot}B(OBu^i){\cdot}OBu^t$. A specimen was converted into the diethanolamine ester of isobutylboronic acid, m. p. and mixed m. p. 155°. The rest was hydrolysed to the boronic acid, m. p. 112°, and dehydrated to the anhydride. The proton magnetic resonance spectrum was identical with that of the authentic material and showed the absence of the t-butyl group.

Attempts to Isolate a Monoperoxide.—The experiments summarised in Table 1 show that the reaction between di-isobutyl-t-butylboron and oxygen (1 mol.) gives a product equivalent to 69% of $Bu^i_2B{\cdot}O{\cdot}OBu^t$ and 31% of $Bu^i{\cdot}B(Bu^t)O{\cdot}OBu^i$. An attempt was made to confirm this composition from the proton magnetic resonance spectrum of a sample prepared by autoxidation in carbon tetrachloride. This appeared to be an appropriate solvent because autoxidation of tri-isobutylboron was known to be slow in this medium, so that the reaction could be stopped at the appropriate stage, and because the absence of hydrogen atoms in the solvent would permit proton resonance spectra to be determined on solutions, perhaps avoiding the redox rearrangement which would occur if attempts were made to isolate the peroxide.

Di-isobutyl-t-butylboron (0·4592 g.) in carbon tetrachloride (55 c.c.) was allowed to absorb 1 mol. of oxygen at the gas-burette. One sample (A) was immediately removed; the bulk of the solvent was removed from the remainder (B) under reduced pressure. The proton magnetic resonance spectra of both samples were similar to that of isobutyl t-butyl isobutylboronate, showing that substantially no peroxide was present; however, sample A, and the carbon tetrachloride which had been removed from B, showed the presence of a new singlet at δ 3·28, in the correct position for t-butyl chloride. The carbon tetrachloride was therefore fractionally distilled, and the presence of t-butyl chloride confirmed in the chromatogram of the first fraction. Carbonyl chloride was also identified by smell, and by the formation of a precipitate of diphenylurea with aniline. Carbonyl chloride was also liberated, but apparently rather more slowly, by a solution of the di(alkylperoxy)boron compound in carbon tetrachloride.

Polymerisation Experiments.—A capsule of tri-s-butylboron (0·2745 g.) was broken under redistilled and outgassed acrylonitrile (15 c.c., 12 g.) under nitrogen (Specimen i). A portion (7 c.c.) was withdrawn into a test-tube open to the air (Specimen ii). Pure di(isobutylperoxy)-isobutylboron (0·1 g.) was added to redistilled and outgassed acrylonitrile (10 c.c., 8 g.) under

TABLE 3. *Polymerisation of acrylonitrile* (*data in min.*).

Specimen	Opalescent	Milky	Pasty	Solid
(i) Bu^s_3B	60	180	—	—
(ii) Bu^s_3B + air	0·5	4	15	21 *
(iii) $Bu^t{\cdot}B(O_2Bu^i)_2$	0·5	3	10	20

* The polymer gave a strong test for peroxide.

nitrogen (Specimen iii). The progress of the polymerisation is shown in Table 3. All three specimens were kept in a thermostat at 24°, but the polymerisation is exothermic: specimen (ii) reached a maximum internal temperature of 36° after 21 min., and specimen (iii) 60° in 10 min.

We are grateful to Professors E. D. Hughes, F.R.S., and Sir Christopher Ingold, F.R.S., for their interest and encouragement.

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[*Received, June 1st,* 1960.]

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61. *The Reactions of Methoxyl Radicals with Cyclopropane and Isobutane.*

By T. Bercés and A. F. Trotman-Dickenson.

The competitive reaction of methoxyl radicals, generated by the pyrolysis of dimethyl peroxide, with ethane and cyclopropane yields

$$\log [k(\text{ethane})/k(\text{cyclopropane})] = -0{\cdot}712 + (2650/2{\cdot}3RT)$$

Absolute rate constants for the transfer reactions of methoxyl radicals have been derived from the study of the consumption of isobutane during the pyrolysis of dimethyl and di-t-butyl peroxide mixtures.

Shaw and Trotman-Dickenson [1] recently measured the relative rates of attack of methoxyl radicals on several hydrocarbons. Methyl nitrate and dimethyl peroxide were decomposed to yield the radicals in a flow system. The results were independent of the source of radicals except for the reactions with cyclopropane. It appeared that the radicals from methyl nitrate were more reactive than those from dimethyl peroxide, which was only used for a few experiments. Shaw and Trotman-Dickenson found cyclopropane to be 0·17 times as reactive as propane at 297°. We have used the same method, and dimethyl peroxide as the source, to compare ethane with cyclopropane between 195° and 324°. The ratio of initial ethane : cyclopropane was varied from 2 : 1 to 1 : 2. The results of eleven runs were evaluated by the method of least squares and gave:

$$\log (A_{\text{ethane}}/A_{\text{cyclopropane}}) = -0{\cdot}712 \pm 0{\cdot}119$$

$$E_{\text{ethane}} - E_{\text{cyclopropane}} = -2680 \pm 290 \text{ cal. mole}^{-1}$$

When combined with the previous results on the ethane–propane system these figures yield

$$k(\text{cyclopropane})/k(\text{propane}) = 0{\cdot}17 \text{ at } 297°$$

in excellent agreement with the result obtained directly. The radicals formed from dimethyl peroxide probably attack cyclopropane only by the hydrogen-abstraction reaction: $CH_3{\cdot}O{\cdot} + C_3H_6 = CH_3{\cdot}OH + C_3H_5{\cdot}$. The reactions that occur with methyl nitrate are unknown. The abstraction of a hydrogen atom from cyclopropane by a methoxyl radical, a methyl radical,[2] a chlorine atom,[3] or the radical involved as chain carrier [4] in oxidations is slower than the abstraction of a typical primary hydrogen atom. It is, therefore, likely that the C–H bond-strength is at least 1—2 units greater than the 97 kcal. mole^{-1} normally allotted to a primary bond.

Trial runs showed that the reactivities of methoxyl radicals with hydrogen and methane could not be studied in this system. Considerable amounts of both gases were formed in the decompositions and subsequent reactions.

Some information on the absolute rates of methoxyl radical reactions has been obtained by analysing the products formed when dimethyl peroxide and di-t-butyl peroxide are decomposed in the flow system with isobutane. The results were interpreted according to the scheme:

$$(MeO)_2 \longrightarrow 2MeO{\cdot} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

$$\left.\begin{array}{l}(Bu^tO)_2 \longrightarrow 2Bu^tO{\cdot} \\ Bu^tO{\cdot} \longrightarrow Me{\cdot} + Me_2CO\end{array}\right\} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

$$Me{\cdot} + CHMe_3 \longrightarrow Bu^t{\cdot} + CH_4 \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (3)$$

$$MeO{\cdot} + CHMe_3 \longrightarrow Bu^t{\cdot} + MeOH \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4)$$

$$MeO{\cdot} + Me{\cdot} \longrightarrow Me_2O \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (5)$$

$$2Me{\cdot} \longrightarrow C_2H_6 \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (6)$$

[1] Shaw and Trotman-Dickenson, *J. Chem. Soc.*, 1960, 3210.
[2] Trotman-Dickenson, "Gas Kinetics," Butterworths, London, 1955.
[3] Knox and Nelson, *Trans. Faraday Soc.*, 1959, **55**, 937.
[4] Falconer, Knox, and Trotman-Dickenson, unpublished results.

The fate of the t-butyl radicals is unknown, but they are comparatively unreactive and are unlikely to re-form isobutane in the presence of higher concentrations of other radicals. Hence we can write:

$$\frac{k_4 k_6^{\frac{1}{2}}}{k_5} = \frac{R_{C_2H_6}}{R_{Me_2O}} \cdot \left(\frac{-R_{CHMe_3}}{R^{\frac{1}{2}}_{C_2H_6}[CHMe_3]} - \frac{k_3}{k_6^{\frac{1}{2}}} \right)$$

where $R_{C_2H_6}$ is the rate of formation of ethane and $[CHMe_3]$ is the mean concentration of isobutane. The rates of formation were found from the known amount of isobutane injected into the system and from the analysis of a known fraction of the products:

$$\log k_6 \text{ (mole}^{-1} \text{ cm.}^3 \text{ sec.}^{-1}) = 13{\cdot}345 \text{ [5]}$$

and

$$\log k_3 \text{ (mole}^{-1} \text{ cm.}^3 \text{ sec.}^{-1}) = 11{\cdot}0 - (7600/2{\cdot}3RT) \text{ (ref. 2)}$$

k_5 has not been measured but can be deduced in two ways.

Hanst and Calvert [6] found, from a study of the decomposition of dimethyl peroxide, that log A_1 (sec.$^{-1}$) = 15·4. The entropy of dimethyl peroxide can be deduced from entropies of *cis*-but-2-ene [7] (71·9) and n-butane (74·1) to be about 73 cal. mole^{-1} deg.$^{-1}$. The entropy of the methoxyl radical has been taken as 54·7 cal. mole^{-1} deg.$^{-1}$ by comparison with the entropy of methyl fluoride (53·3). Hence log A_{-1} (mole^{-1} cm.^{3} sec.$^{-1}$) = 13·0. The rate constants for the combination of unlike small radicals in the gas phase have been found to be very close to twice the geometric means of the rate constants for the combination of the two like radicals for almost all the systems studied.[8] Hence $k_5 = 2(k_{-1}k_6)^{\frac{1}{2}}$. If none of the reactions has an activation energy, then:

$$\log k_5 \text{ (mole}^{-1} \text{ cm.}^3 \text{ sec.}^{-1}) = 13{\cdot}5$$

An alternative value can be derived from Benson and Jain's value [9] of log A_{-5} (sec.$^{-1}$) = 18·1, and considerations of the entropy change similar to those given above. Then log k_5 (mole^{-1} cm.^{3} sec.$^{-1}$) = 14·6. This value is probably not reliable, as A_{-5} was deduced from a complicated scheme for the chain decomposition of dimethyl ether and was not measured directly.

TABLE 1. *The pyrolysis of dimethyl and di-t-butyl peroxide in isobutane* (R in mole c.c.$^{-1}$ sec.$^{-1}$).

Temp.	10^7 [$CHMe_3$] (average) (mole c.c.$^{-1}$)	$10^{10}R_{CHMe_3}$	$10^{10}R_{C_2H_6}$	$10^{10}R_{C_2H_6O}$	$10^{-9}k_4$
190·5°	2·25	1·81	1·65	0·30	2·12
192·5	2·44	1·75	1·37	0·27	1·93
193·0	2·00	1·69	1·67	0·30	2·55
211·0	2·00	4·53	3·15	0·69	3·65
211·0	1·83	3·23	2·97	0·69	2·75
212·0	1·97	3·77	0·95	0·39	3·06
219·0 [a]	3·17	16·29	8·77	2·78	3·90
221·0	2·11	4·23	3·17	0·77	2·98
221·5	1·98	3·97	3·62	0·73	3·27
229·0	2·53	3·95	1·81	0·76	2·82
235·0 [a]	3·23	23·13	19·19	4·10	4·80
241·0	2·55	4·53	3·29	0·51	3·80
242·0	2·29	7·94	3·20	0·56	3·01
257·0	2·64	5·70	2·10	0·47	4·07
260·0 [a]	3·08	27·50	19·20	4·34	5·61

[a] Run in small reaction vessel.

[5] Shepp, *J. Chem. Phys.*, 1956, **24**, 939.
[6] Hanst and Calvert, *J. Phys. Chem.*, 1959, **63**, 104.
[7] Entropies are taken from "Selected Values of Thermodynamic Properties," Circular 500, National Bureau of Standards, Washington, 1952.
[8] Trotman-Dickenson, *Ann. Rev. Phys. Chem.*, 1959, **10**, 53.
[9] Benson and Jain, *J. Chem. Phys.*, 1959, **31**, 1008.

The experimental conditions and results are summarised in Table 1, together with values of k_4 deduced from the first value of k_5. The dependence of k_4 on the volume of the reaction vessel is smaller than was expected, in view of the fact that the mean residence time of a molecule is equal to the half-life of one of the radical sources at 200° for the large and 225° for the small (one-sixth the size) reaction vessel. The results in the large and small vessels are sufficiently similar to justify confidence in the rate constants around 200°. The Arrhenius equation found with the large vessel was

$$\log k_4 \text{ (mole}^{-1} \text{ cm.}^3 \text{ sec.}^{-1}) = (11{\cdot}30 \pm 0{\cdot}24) - (4100 \pm 600)/2{\cdot}3RT$$

A_4 is of the normal magnitude for the reaction of a small radical with a moderate sized molecule. E_4 is about 3 kcal. mole^{-1} lower than the activation energy for the attack of a methyl radical on isobutane. This higher reactivity is in keeping with the lower selectivity of methoxyl radicals.[1] As has previously been pointed out, Wijnen's results [10] on the photolysis of methyl acetate can be interpreted to yield an activation energy of 7·1 kcal. mole^{-1} for the attack of methoxyl radicals on methyl acetate, as compared with 10 kcal. mole^{-1} for attack by methyl. If the present value of k_5 is accepted the A factor for the attack on methyl acetate by methoxyl is $10^{11{\cdot}6}$ mole^{-1} cm.^{3} sec.$^{-1}$ which is in line with those for the hydrocarbons shown in Table 2. The results form a self-consistent pattern except that the activation energy for n-butane appears slightly low (there is no corresponding discrepancy in the rate constant; therefore it is likely that the low value is the consequence of experimental error).

TABLE 2. *Reaction of methoxyl radicals with hydrocarbons.*

Hydrocarbon	log A (mole^{-1} cm.^{3} sec.$^{-1}$)	E (kcal. mole^{-1})	$10^{-8}k$ (250°) (mole^{-1} cm.^{3} sec.$^{-1}$)	Hydrocarbon	log A (mole^{-1} cm.^{3} sec.$^{-1}$)	E (kcal. mole^{-1})	$10^{-8}k$ (250°) (mole^{-1} cm.^{3} sec.$^{-1}$)
Ethane	11·8	7·1	7	Isobutane	11·3	4·1	38
Propane	11·6	5·2	24	Neopentane	12·1	7·3	11
n-Butane	10·8	2·9	40	Cyclopropane	12·5	9·7	3

Experimental.—The apparatus and procedure used to study the competitive attack on ethane and cyclopropane were identical with those used by Shaw and Trotman-Dickenson.[1] They were slightly modified in the experiments with isobutane to allow the injection of known amounts of di-t-butyl peroxide into the gas stream. A thermal-conductivity cell was used as a detector for the gas chromatography. In three experiments the 150 c.c. reaction vessel was replaced by one of 24 c.c. with 2 mm. capillary connecting tubes.

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CHEMISTRY DEPARTMENT, EDINBURGH UNIVERSITY. [*Received, July 18th,* 1960.]

[10] Wijnen, *J. Chem. Phys.*, 1957, **27**, 712.

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62. *A New Synthesis of Long-chain Acetylenic Acids and Some Attempts to Prepare Pure* cis*-Olefinic Acids.*

By D. E. Ames and (in part) P. J. Islip.

The *NN*-dimethylamide of a long-chain acetylenic acid is prepared by condensation of an ω-acetylenic dimethylamide and alkyl halide (or ω-bromo-dimethylamide and alkylacetylene) in presence of sodamide in liquid ammonia.

Conversion of dihydroxy-acids into dibromo-esters, followed by debromination, gives *cis*-olefinic acids containing *ca.* 2% of the *trans*-isomers. Attempts to avoid the formation of the latter failed.

Although many syntheses of long-chain acetylenic acids have been described,[1] the accessible ω-bromo- and ω-acetylenic acids have rarely been used as starting materials. Bhattacharya, Saletore, and Simonsen [2] condensed sodiodec-1-yne with ethyl 12-bromododecanoate in xylene at 160° and after hydrolysis obtained docos-13-ynoic acid in unspecified yield. A very similar procedure was employed recently by Bhattacharyya, Chakravarty, and Kumar [3] to condense ethyl undec-10-ynoate with alkyl halides (yields about 15% after hydrogenation and hydrolysis). Alkylation of methyl undec-10-ynoate by treatment of the silver derivative with methyl and ethyl iodide was achieved by Isabelle and Leitch,[4] but we have been unable to alkylate the silver derivative of ethyl undec-10-ynoate with octyl bromide.

$H{\cdot}C{\equiv}C{\cdot}[CH_2]_8{\cdot}CO{\cdot}NMe_2$ (I) $\quad C_8H_{17}{\cdot}C{\equiv}C{\cdot}[CH_2]_8{\cdot}COR$ (II) $\quad C_8H_{17}{\cdot}\overset{cis}{CH{=}CH}{\cdot}[CH_2]_8{\cdot}CO{\cdot}NMe_2$ (III)

$C_8H_{17}{\cdot}CH(OH){\cdot}CH(OH){\cdot}[CH_2]_8{\cdot}COR$ (IVa) *threo*; (IVb) *erythro*

$C_8H_{17}{\cdot}CHBr{\cdot}CHBr{\cdot}[CH_2]_8{\cdot}CO_2Et$ (Va) *erythro*; (Vb) *threo*

$C_8H_{17}{\cdot}CH{=}CH{\cdot}[CH_2]_8{\cdot}COR$ (VIa) *trans*; (VIb) *cis*

In the present work, advantage was taken of the resistance shown by the *NN*-dimethylamide group to many organometallic reagents. Thus *NN*-dimethylundec-10-ynamide (I), on treatment with sodamide in liquid ammonia, gave the sodio-derivative from which the amide could be recovered in good yield. Octyl bromide reacted with this sodio-derivative, to give *NN*-dimethylnonadec-10-ynamide (II; R = NMe_2) in 62% yield. Alkaline hydrolysis afforded nonadec-10-ynoic acid (II; R = OH).

Selective hydrogenation of the acetylenic amide by Cram and Allinger's procedure [5] gave *cis-NN*-dimethylnonadec-10-enamide (III) containing ~2% of the *trans*-isomer (estimate based on the intensity of *trans*-HC=CH band at 966 cm.$^{-1}$). Epoxidation with perbenzoic acid, cleavage of the oxide ring with formic acid, and mild alkaline hydrolysis afforded *threo*-10,11-dihydroxy-*NN*-dimethylnonadecanamide (IVa; R = NMe_2). More vigorous alkaline hydrolysis gave the acid (IVa; R = OH) which was converted into the dibromo-ester (Va) and thence into *trans*-nonadec-10-enoic acid (VIa). As an alternative route to the *trans*-acid, reduction of amide (II; R = NMe_2) with sodium in liquid ammonia was examined (cf. the preparation of the octadecenes by Elsner and Paul [6]). The only product isolated was *trans*-nonadec-10-enamide (VIa; R = NH_2); that is, ammonolysis occurred during the reduction though not during the original synthesis of dimethylamide (II).

In an attempt to obtain *cis*-nonadec-10-enoic acid free from the *trans*-isomer, its

[1] *Inter al.*, Bumpus, Taylor, and Strong, *J. Amer. Chem. Soc.*, 1950, **72**, 4263; Huber, *ibid.*, 1951, **73**, 2730.
[2] R. Bhattacharya, Saletore, and Simonsen, *J.*, 1928, 2678.
[3] S. C. Bhattacharyya, Chakravarty, and Kumar, *Chem. and Ind.*, 1959, 1352.
[4] Isabelle and Leitch, *Canad. J. Chem.*, 1958, **36**, 440.
[5] Cram and Allinger, *J. Amer. Chem. Soc.*, 1956, **78**, 2522.
[6] Elsner and Paul, *J.*, 1953, 3156.

purification through the crystalline *erythro*-10,11-dihydroxynonadecanoic acid (IVb; R = OH) was examined.[7] *cis*-Hydroxylation of the semihydrogenation product (III) with iodine and silver acetate in moist acetic acid,[8] followed by mild hydrolysis, gave the amide (VIb; R = NMe_2), and vigorous hydrolysis then furnished the *erythro*-dihydroxy-acid (VIb; R = OH). This was converted by standard procedures [7] through dibromo-ester (Vb) into ethyl *cis*-nonadec-10-enoate which again contained ~2% of *trans*-isomer, even when the intermediate dihydroxy-acid was most carefully purified. Re-examination of samples of ethyl oleate and *cis*-heptadec-9-enoate prepared previously by this procedure [7] and believed to be pure showed that these also contained ~2% of the *trans*-isomers. The absorption band at *ca.* 966 cm.$^{-1}$ provides a sensitive method for detecting *trans*-isomer in *cis*-esters and -dimethylamides, whereas in the acids this band is partially masked by a broad carboxyl band.

The presence of some *trans*-isomer in these products indicates that conversion of diol into dibromide or debromination (or both steps) is not completely stereospecific. To determine at which step the isomeric product was formed, the use of a crystalline dibromide was considered. Since the 9,10-dibromo-octadecanoic acids are very low-melting, the tetrabromide obtained by addition of bromine to linoleic acid was used. Esterification, followed by debromination with zinc, gave ethyl linoleate containing about 5% of *trans*-isomers (McCutcheon's debromination procedure [9] gave similar results). The presence of *trans*-isomers in methyl linoleate obtained from the tetrabromo-acid has been reported by Hosking.[10] Thus the debromination step is not completely stereospecific (present evidence does not show whether the conversion of diol into dibromide is completely stereospecific).

$MeO{\cdot}[CH_2]_5{\cdot}COMe$ (VII) $\quad MeO{\cdot}[CH_2]_5{\cdot}CMe{=}C(CN){\cdot}CO_2Et$ (VIII) $\quad MeO{\cdot}[CH_2]_5{\cdot}CMe_2{\cdot}CH_2{\cdot}CN$ (IX)

$Br{\cdot}[CH_2]_5{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$ (X) $\quad C_8H_{17}{\cdot}C{\equiv}C{\cdot}[CH_2]_5{\cdot}CMe_2{\cdot}CH_2{\cdot}CO{\cdot}NMe_2$ (XI)

$C_8H_{17}{\cdot}CH{=}^{cis}CH{\cdot}[CH_2]_5{\cdot}CMe_2{\cdot}CH_2{\cdot}CO_2H$ (XII)

Dr. J. W. Cornforth, who recently developed a stereospecific synthesis of olefins,[11] kindly discussed this problem and suggested that debromination in the presence of base might prevent the formation of *trans*-isomer, if this side-reaction were due to zinc ions' acting as Lewis acids. Debromination of ethyl di- and tetra-bromo-octadecanoate was therefore carried out in the presence of sodium acetate, pyridine, and ethylenediamine-tetra-acetic acid severally, but in each case the *trans*-isomer was formed in about the same proportion as in the previous experiments.

A pure sample of *cis*-nonadec-10-enoic acid was ultimately obtained from the semi-hydrogenation product by treatment with urea.[12]

cis-3,3-Dimethyloctadec-9-enoic acid (XII) was also synthesised by a route similar to that described above, but in this case an ω-bromo-dimethylamide was condensed with the sodio-derivative of an alkylacetylene. 7-Methoxyheptan-2-one (VII), from 4-methoxy-butyl bromide and ethyl acetoacetate, was condensed with ethyl cyanoacetate.[13] Addition of methylmagnesium iodide to the unsaturated cyano-ester (VIII), followed by hydrolysis and decarboxylation, gave methoxy-nitrile (IX), and thence 8-methoxy-3,3-dimethyl-octanoic acid. Treatment with hydrobromic and sulphuric acid gave the 8-bromo-acid (X); the dimethylamide of this was condensed with sodiodec-1-yne, and the resulting amide

[7] Ames and Bowman, *J.*, 1951, 1079; Bounds, Linstead, and Weedon, *J.*, 1953, 2393.
[8] Gunstone and Morris, *J.*, 1957, 487.
[9] McCutcheon, *Org. Synth.*, Coll. Vol. III, p. 526.
[10] Hosking, quoted by Ackman, Dytham, Wakefield, and Weedon, *Tetrahedron*, 1960, **8**, 244.
[11] Cornforth, Cornforth, and Mathew, *J.*, 1959, 112.
[12] Cf. Crombie and Griffin, *J.*, 1958, 4443.
[13] Cope, Hofmann, Wyckoff, and Hardenbergh, *J. Amer. Chem. Soc.*, 1941, **63**, 3452.

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(XI) was semihydrogenated and hydrolysed to *cis*-3,3-dimethyloctadec-9-enoic acid (containing small amounts of *trans*- and saturated acids).

Experimental

NN-*Dimethylundec*-10-*ynamide*.—Undec-10-ynoic acid [14] (170 g.) was warmed with thionyl chloride (230 c.c.) for 3 hr. at 70°. After the excess of thionyl chloride had been removed under reduced pressure, ether (1 l.) was added and dimethylamine was passed into the solution until the latter was alkaline. Water (1 l.) was added and the separated organic layer was washed with sodium carbonate solution and water, dried (Na_2SO_4), and distilled. The *amide* (177 g.), b. p. 125—130°/1 mm., formed prisms, m. p. 30—31°, from light petroleum (b. p. 40—60°) (Found: C, 74·9; H, 11·4; N, 6·6. $C_{13}H_{23}NO$ requires C, 74·6; H, 11·1; N, 6·7%).

NN-*Dimethylnonadec*-10-*ynamide*.—Sodamide (27 g.; commercial, crystalline material, supplied by Messrs. May and Baker, gave about the same yield as sodamide prepared *in situ*) was stirred with liquid ammonia (1 l.) for 5 min. and the acetylenic amide (140 g.) in ether (150 c.c.) was added gradually. After the mixture had been stirred for 1 hr., octyl bromide (180 g.) in ether (150 c.c.) was added slowly; the mixture was stirred under reflux for 5 hr. and then allowed to evaporate. Dilute hydrochloric acid (1 l.) was added and the product isolated with ether. Fractional distillation gave the *amide* (133 g.), b. p. 172—175°/0·1 mm., n_D^{20} 1·4725 (Found: C, 78·5; H, 12·5; N, 4·4. $C_{21}H_{39}NO$ requires C, 78·4; H, 12·2; N, 4·4%), $\nu_{max.}$ 1644 cm.$^{-1}$ ($CO{\cdot}NMe_2$).

Nonadec-10-*ynoic Acid*.—The dimethylamide (10 g.) was refluxed in ethanol (150 c.c.) and 5N-sodium hydroxide (150 c.c.) for 8 hr. Water (150 c.c.) was added and the ethanol removed by distillation; the solution was poured into ice and dilute sulphuric acid and extracted with ether. Distillation gave the *acid*, b. p. 174—176°/0·2 mm., plates (from methanol), m. p. 43—44° (Found: C, 78·0; H, 11·3. $C_{19}H_{34}O_2$ requires C, 77·5; H, 11·6%).

Semihydrogenation of NN-*Dimethylnonadec*-10-*ynamide*.—The acetylene (31·5 g.) in methanol (200 c.c.) was hydrogenated in presence of 5% palladised barium sulphate (0·5 g.) and quinoline [5] (0·5 g.). When 1·05 mol. had been taken up, the rate of absorption fell rapidly and hydrogenation was interrupted. Distillation of the filtered solution afforded cis-NN-*dimethylnonadec*-10-*enamide* (29 g.), b. p. 164—167°/0·1 mm., n_D^{20} 1·4682 (Found: C, 78·2; H, 13·2; N, 4·2. $C_{21}H_{41}ON$ requires C, 78·0; H, 12·8; N, 4·3%), $\nu_{max.}$ 966 cm.$^{-1}$ (vw, corresponding to *ca.* 2% of *trans*-isomer).

threo-10,11-*Dihydroxy*-NN-*dimethylnonadecanamide*.—The olefin (14·1 g.) in chloroform (50 c.c.) was added gradually to 0·56M-perbenzoic acid (100 c.c.) in chloroform at 0°. After 1 hr., 96% of the peracid had reacted and the solution was washed with sodium carbonate solution and water and evaporated *in vacuo*. 98% Formic acid (50 c.c.) was added to the residue which was left overnight and then re-evaporated. The residue was refluxed with ethanol (100 c.c.) and 2N-sodium hydroxide (50 c.c.) for 1 hr.; acidification, followed by isolation with ethyl acetate, furnished the dihydroxy-amide (10·0 g.), prisms, m. p. 65—66° (from ethyl acetate) (Found: C, 70·2; H, 12·5; N, 3·9. $C_{21}H_{43}NO_3$ requires C, 70·5; H, 12·1; N, 3·9%).

threo-10,11-*Dihydroxynonadecanoic Acid*.—The amide (4·8 g.) in 2-methoxyethanol (50 c.c.) with potassium hydroxide (5 g.) in water (5 c.c.) was heated at 170° for 6 hr. under nitrogen. After the hot solution had been poured into ice and 2N-hydrochloric acid, the precipitated *acid* was recrystallised from ethyl acetate, forming plates, m. p. 93·5—94·5° (4·3 g.) (Found: C, 68·8; H, 11·6. $C_{19}H_{38}O_4$ requires C, 69·0; H, 11·6%).

Ethyl trans-*Nonadec*-10-*enoate*.—Treatment of the dihydroxy-acid (11·6 g.) with hydrogen bromide in acetic and sulphuric acid, esterification, and debromination of the dibromo-ester (which was not distilled) were carried out by general procedures.[7] The unsaturated *ester* (7·7 g.) had b. p. 144—146°/0·1 mm., n_D^{20} 1·4526 (Found: C, 77·7; H, 12·5%; I val., 77·3, 78·0. $C_{21}H_{40}O_2$ requires C, 77·7; H, 12·4%; I val., 78·2).

trans-*Nonadec*-10-*enoic Acid*.—A solution of the ester (7·3 g.) in ethanol (70 c.c.) was refluxed with potassium hydroxide (5 g.) in water (20 c.c.) under nitrogen for 1·5 hr. After addition of water (80 c.c.), ethanol was removed by distillation; acidification and isolation with ether yielded the *acid* (6·6 g.), plates, m. p. 49—50° [from light petroleum (b. p. 40—60°)] (Found: C, 77·5; H, 12·5%; I val., 85·1, 84·7. $C_{19}H_{36}O_2$ requires C, 77·0; H, 12·2%; I val., 85·6).

trans-*Nonadec*-10-*enamide*.—*NN*-Dimethylundec-10-ynamide (10 g.) in ether (100 c.c.) was

[14] Kraft and Popova, *Zhur. obshchei Khim.*, 1957, **27**, 906.

added during 5 min. to a stirred solution of sodium (4·4 g.) in liquid ammonia (400 c.c.). The solution was stirred under reflux for 4 hr., then allowed to evaporate. Ether–methanol and then dilute acetic acid were added cautiously, and the mixture was extracted with ether. The extracts were washed with dilute sulphuric acid, sodium carbonate solution, and water, dried (Na_2SO_4), and evaporated. Recrystallisation from methanol gave the *amide* (3·8 g.), prisms, m. p. 79—81° (Found: C, 77·5; H, 12·4; N, 5·1. $C_{19}H_{37}NO$ requires C, 77·2; H, 12·6; N, 4·7%).

Hydrolysis of the amide (0·5 g.) by refluxing with 2-methoxyethanol (25 c.c.) and potassium hydroxide (5 g.) in water (5 c.c.) for 2 hr. and pouring the product into ice and dilute acid, gave *trans*-nonadec-10-enoic acid, m. p. 48—49°, identical with the sample prepared above.

erythro-10,11-*Dihydroxy*-NN-*dimethylnonadecanamide*.—*cis*-NN-Dimethylnonadec-10-enamide (5·0 g.; semihydrogenation product) was shaken for 30 min. with iodine (4·1 g.), silver acetate (5·8 g.), and acetic acid (150 c.c.). After addition of water (0·3 g.), the mixture was refluxed for 1 hr., cooled, and filtered, the solid being washed with acetic acid. The combined filtrates were evaporated under reduced pressure and the residue was taken up in ether, washed with 2N-sodium hydroxide and water, dried (Na_2SO_4), and evaporated. The residual gum was refluxed for 2 hr. with 5N-sodium hydroxide (25 c.c.) and ethanol (50 c.c.), and the solution was then poured into ice and sulphuric acid. Isolation with chloroform, followed by recrystallisation from ethyl acetate, gave the *dihydroxy-amide* (2·0 g.), prisms, m. p. 95—97° (Found: C, 70·6; H, 12·2; N, 3·7%).

erythro-10,11-*Dihydroxynonadecanoic Acid*.—The acetylenic amide (17·7 g.) was semi-hydrogenated and hydroxylated as in the preceding experiment. The crude product was refluxed for 10 hr. with ethanol (50 c.c.) and 5N-sodium hydroxide (50 c.c.); the precipitate formed on acidification was recrystallised from ethyl acetate and methanol to give the *dihydroxy-acid* (8·6 g.), prisms, m. p. 118·5—119·5° (Found: C, 68·8; H, 11·7%).

cis-*Nonadec*-10-*enoic Acid*.—The *erythro*-dihydroxy-acid (7·8 g.) was converted into the dibromo-ester (which was not distilled) and thence into *ethyl* cis-*nonadec*-10-*enoate* by the general procedures.[7] The ester (6·1 g.) had b. p. 156—158°/0·4 mm., n_D^{20} 1·4518 (Found: C, 77·4; H, 12·2%; I val., 78·3). It contained about 2% of *trans*-isomer (band at 969 cm.$^{-1}$).

A solution of the ester (5·7 g.) in ethanol (60 c.c.) and potassium hydroxide (5 g.) in water (5 c.c.) was refluxed under nitrogen for 1·5 hr. After addition of water (120 c.c.), ethanol was removed by distillation and the product was isolated from the acidified solution with ether. Distillation in nitrogen gave the *acid* (5·4 g.), b. p. 184—186°/0·5 mm., n_D^{20} 1·4609, f. p. (thermometer in liquid) 20·5—21·5° (Found: C, 77·1; H, 12·6%; I val., 86·1).

Purification of cis-*Nonadec*-10-*enoic Acid with Urea*.—The acetylenic acid (6·5 g.) in methanol (75 c.c.) was hydrogenated in presence of 5% palladised barium sulphate (0·2 g.) and quinoline (0·2 g.). Absorption became very slow when 1·06 mol. of hydrogen had been taken up; hydrogenation was interrupted and the filtered solution was diluted to 500 c.c. with ethanol. Urea (60 g.) was dissolved in the hot solution and the mixture allowed to crystallise by cooling. After filtration, more urea (20 g.) was added, and the solution allowed to crystallise again. The filtrate was poured into 0·3N-sulphuric acid (1·2 l.) and extracted with ether–light petroleum (b. p. 40—60°) (1 : 1; 3 × 300 c.c.). The washed, dried (Na_2SO_4) extracts were distilled, to give the acid (1·4 g.), m. p. 22—23° (sealed capillary), b. p. 170—175°/0·2 mm. (Found: I val., 84·6). This sample had no shoulder corresponding to *trans*-HC=CH absorption, whereas the previous sample had a slight shoulder at *ca.* 970 cm.$^{-1}$.

Debromination Experiments (with P. J. Islip).—These were carried out essentially as described by Ames and Bowman.[7] In a typical experiment, zinc (7·5 g.) was activated by heating it with ethanol to the b. p., adding 0·1 c.c. of 48% hydrobromic acid, and refluxing under nitrogen for 5 min. Anhydrous sodium acetate (4·7 g., 6 mol.) and then ethyl *threo*-9,10-dibromo-octadecanoate (4·5 g., 1 mol.) in ethanol (10 c.c.) were added, and the mixture was refluxed for 1 hr. The zinc was collected and washed with light petroleum (b. p. 40—60°); after the combined filtrates had been poured into dilute sulphuric acid, the organic layer was washed with sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and distilled in nitrogen. The ethyl oleate (1·4 g.) obtained contained about 2% of *trans*-isomer.

Similar experiments with ethylenediaminetetra-acetic acid and pyridine (even 1 : 1 pyridine–ethanol as solvent) did not affect the proportion of *trans*-isomer significantly. Debromination of ethyl 9,10,12,13-tetrabromoctadecanoate gave ethyl linoleate containing about 5% of *trans*-isomers (band at 967 cm.$^{-1}$).

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7-Methoxyheptan-2-one.—4-Methoxybutyl bromide [15] (450 g.) was added during 20 min. to ethyl sodioacetoacetate solution (from sodium 78 g., ethyl acetoacetate 480 g., and ethanol 1250 c.c.). The solution was stirred under reflux (bath 110°) for 6 hr. and ethanol (1 l.) was removed by distillation. 1·3N-Sodium hydroxide (3 l.) was added to the residue, and the mixture stirred at room temperature for 18 hr. After addition of 20N-sulphuric acid (300 c.c.) during 2·5 hr., the mixture was heated slowly to the b. p. and then refluxed for 1 hr. The product was isolated with ether and fractionally distilled through a short Fenske column; the slightly impure ketone (260 g.) had b. p. 95—100°/20 mm. (Found: C, 67·5; H, 11·3. Calc. for $C_8H_{16}O_2$: C, 66·6; H, 11·2%).

Ethyl 2-Cyano-8-methoxy-3-methyloct-2-enoate.—A mixture of methoxy-ketone (260 g.), ethyl cyanoacetate (210 g.), benzene (170 c.c.), acetic acid (21 g.), and ammonium acetate (13 g.) was refluxed through a phase-separator until no more water was collected.[13] The cooled solution was washed with sodium carbonate solution and water, dried (Na_2SO_4), and evaporated. Fractional distillation gave the cyano-ester (362 g.), b. p. 140—145°/2 mm., n_D^{20} 1·4706 (Found: C, 65·5; H, 8·9; N, 6·1. $C_{13}H_{21}NO_3$ requires C, 65·2; H, 8·9; N, 5·9%). A fore-run, b. p. 70—140°/2 mm., was re-treated with ethyl cyanoacetate to afford more product (31 g.).

Ethyl 2-Cyano-8-methoxy-3,3-dimethyloctanoate.—The Grignard reagent (from magnesium 53 g., and methyl iodide 320 g., in ether 1 l.) was stirred and cooled in ice-water while the cyano-ester (362 g.) in ether (750 c.c.) was added.[16] Next day, ammonium chloride solution and acetic acid were added and the crude product was isolated with ether. The residue was left for 2 days with sodium cyanide (75 g.) in water (250 c.c.) and ethanol (750 c.c.). After addition of water (2 l.), the mixture was extracted thrice with ethyl acetate; the combined extracts were washed with sodium carbonate solution and water, evaporated, and distilled. The *cyano-ester* (273 g.) had b. p. 125—130°/0·8 mm., n_D^{20} 1·4488 (Found: C, 66·4; H, 9·9; N, 5·5. $C_{14}H_{25}NO_3$ requires C, 65·9; H, 9·9; N, 5·5%).

8-Methoxy-3,3-dimethyloctanonitrile.—Potassium hydroxide (120 g.) in water (120 c.c.) was added to the cyano-ester (273 g.) in ethanol (1 l.), and the solution was refluxed for 1 hr. After addition of water (500 c.c.), the solution was concentrated to 1 l. under reduced pressure. Acidification and isolation with ethyl acetate gave crude cyano-acid which was heated (bath 210—240°) with glass powder (1 g.) until decarboxylation ceased (1·5 hr.). Distillation gave the *nitrile* (180 g.), b. p. 75—80°/0·15 mm., n_D^{20} 1·4398 (Found: C, 72·5; H, 11·4; N, 7·1. $C_{11}H_{21}NO$ requires C, 72·1; H, 11·6; N, 7·6%).

8-Methoxy-3,3-dimethyloctanoic Acid.—When the nitrile (180 g.) in ethylene glycol (1 l.) was refluxed (bath 190°) with potassium hydroxide (180 g.) in water (180 c.c.); evolution of ammonia was slow. Water was removed by distillation, and the residue refluxed (bath 230°) for 30 hr. and then poured into 2N-hydrochloric acid (3·6 l.). Isolated with ether, the *acid* (187 g.) had b. p. 114—116°/0·2 mm., n_D^{20} 1·4460 (Found: C, 65·6; H, 11·2. $C_{11}H_{22}O_3$ requires C, 65·3; H, 11·0%).

8-Bromo-3,3-dimethyloctanoic Acid.—Concentrated sulphuric acid (100 c.c.) was added gradually to a mixture of methoxy-acid (187 g.) and 48% hydrobromic acid (450 c.c.). The solution was refluxed for 7 hr. (bath 170°), more hydrobromic acid (100 c.c.) being added after 5 hr. After the mixture had been poured into water (2 l.) and extracted repeatedly with ethyl acetate, the combined extracts were washed with water and evaporated. Distillation furnished the *bromo-acid* (145 g.), b. p. 130—133°/0·4 mm., n_D^{20} 1·4790 (Found: C, 47·4; H, 7·6; Br, 32·4. $C_{10}H_{19}BrO_2$ requires C, 47·8; H, 7·6; Br, 31·8%).

A substantial residue from the distillation (presumably polymeric esters of the hydroxy-acid) was re-treated with hydrobromic acid (200 c.c.) and sulphuric acid (50 c.c.) and gave a further 42 g. of bromo-acid.

8-Bromo-3,3,N,N-tetramethyloctanamide.—The acid (20 g.) was refluxed with thionyl chloride (25 c.c.) for 2 hr. and excess of thionyl chloride was removed under reduced pressure. Ether (200 c.c.) was added and the solution was stirred and cooled (ice-water) while dimethylamine was passed in until the exothermic reaction ceased. Water (50 c.c.) was added and the separated aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with sodium carbonate solution (50 c.c.), dried (Na_2SO_4), and distilled. The *bromo-amide* (14 g.) had b. p. 110—114°/0·3 mm., n_D^{20} 1·4888 (Found: C, 52·3; H, 9·0; N, 4·7; Br, 28·0. $C_{12}H_{24}BrNO$ requires C, 51·8; H, 8·7; N, 5·0; Br, 28·7%).

[15] Schmidt, *Helv. Chim. Acta*, 1944, **27**, 127.
[16] Cf. Prout, *J. Amer. Chem. Soc.*, 1952, **74**, 5916; Parker and Raphael, *J.*, 1955, 1724.

3,3,N,N-*Tetramethyloctadec-9-ynamide*.—Dec-1-yne (28 g.) in tetrahydrofuran (50 c.c.; dried over lithium aluminium hydride) was added gradually to a suspension of sodamide (7·8 g.) in liquid ammonia (250 c.c.). After the mixture had been stirred under reflux for 1 hr., the bromo-amide (49 g.) in tetrahydrofuran (50 c.c.) was added, and the whole was refluxed for 4 hr. and then allowed to evaporate. Water (800 c.c.) was added and the product isolated with ethyl acetate. Fractional distillation gave crude acetylenic *amide*, b. p. 175—190°/0·5 mm., containing a small amount of crystalline solid, apparently dimethylamine hydrobromide. This was removed by washing with water and the oil was redistilled to afford an almost colourless oil (25·8 g.), b. p. 164—166°/0·1 mm., n_D^{20} 1·4739 (Found: C, 78·2; H, 12·3; N, 4·5. $C_{22}H_{41}NO$ requires C, 78·7; H, 12·3; N, 4·2%).

cis-3,3-*Dimethyloctadec-9-enoic Acid*.—A mixture of the foregoing acetylenic amide (10·2 g.), ethanol (80 c.c.), 5% palladised barium sulphate (0·2 g.), and quinoline (0·2 g.) was hydrogenated. The rate of absorption fell sharply at *ca.* 1·0 mol. and hydrogenation was interrupted when 1·05 mol. had been taken up. Distillation of the filtered solution gave cis-3,3,N,N-*tetramethyloctadec-9-enamide* (9·3 g.), b. p. 155—158°/0·1 mm., n_D^{20} 1·4702 (Found: C, 77·9; H, 12·8; N, 3·8. $C_{22}H_{43}ON$ requires C, 78·3; H, 12·8; N, 4·2%).

This amide (7·8 g.), potassium hydroxide (10 g.) in water (10 c.c.), and ethylene glycol (100 c.c.) were distilled until the water had been removed. The solution was refluxed under nitrogen (bath 220°) for 24 hr. and then poured into 2N-hydrochloric acid (650 c.c.). The *acid* (6·5 g.), isolated with ethyl acetate, had b. p. 166—170°/0·2 mm., n_D^{20} 1·4619 (Found: C, 77·5; H, 12·3%; I val., 77·8, 78·0. $C_{20}H_{38}O_2$ requires C, 77·4; H, 12·3%; I val., 81·2).

3,3-*Dimethyloctadecanoic Acid*.—The acetylenic amide (6·0 g.) in ethanol (50 c.c.) was hydrogenated with 5% palladised charcoal (1 g.) until absorption ceased. Evaporation of the filtered solution gave a gum which was hydrolysed as in the preceding experiment. The acid (5·2 g.), b. p. 173—176°/0·4 mm., m. p. 42—43°, recrystallised from light petroleum (b. p. 40—60°) and then had m. p. 43—44°. Cason, Sumrell, and Mitchell [17] report m. p. 44·0—44·8°.

We thank Drs. R. E. Bowman and J. F. McGhie for helpful discussions, Miss E. M. Tanner for the spectroscopic data, and Mr. F. Oliver for microanalyses.

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[*Received, August 19th*, 1960.]

[17] Cason, Sumrell, and Mitchell, *J. Org. Chem.*, 1950, **15**, 850.

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63. *Diboron Tetrachloride–Olefin Compounds. Part III.*[1] *The Reaction of Diboron Tetrachloride with Trichloroethylene, Isobutene, and* cis- *and* trans-*But-2-ene.*

By J. FEENEY, A. K. HOLLIDAY, and F. J. MARSDEN.

Diboron tetrachloride is stabilised by addition of trichloroethylene; the nuclear magnetic resonance spectrum of the mixture indicates adduct formation, but no adduct was isolated. Diboron tetrachloride causes polymerisation of isobutene but forms stable 1 : 1 adducts with *cis*- and *trans*-but-2-ene. Both of these react with trimethylamine and ammonia in the same way as the ethylene adduct, but oxidation gives 2-chlorobutane and no free olefin. The wide melting ranges of these adducts are attributed to mixtures of rotational isomers, on the basis of their nuclear magnetic resonance spectra.

SINCE the isolation [2] of ethylene-1,2-bis(boron dichloride) $Cl_2B{\cdot}CH_2{\cdot}CH_2{\cdot}BCl_2$, the preparation and properties of other diboron tetrachloride–olefin adducts have been described,[3] *e.g.*, the stable but-2-ene adduct B_2Cl_4,CHMe:CHMe; but halogenoethylenes do not appear

[1] Part I, *J.*, 1960, **43**; Part II, *J.*, 1960, 2075.
[2] Urry, Kerrigan, Parsons, and Schlesinger, *J. Amer. Chem. Soc.*, 1954, **76**, 5299.
[3] Ceron, Finch, Frey, Kerrigan, Parsons, Urry, and Schlesinger, *J. Amer. Chem. Soc.*, 1959, **81**, 6368.

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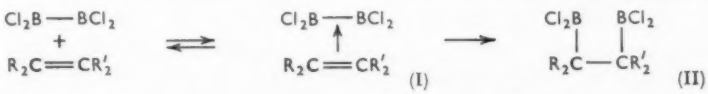
to react with diboron tetrachloride, although they stabilise it against decomposition to polymeric $(BCl)_n$ and boron trichloride.

The rapidity of the reaction of many olefins with diboron tetrachloride at low temperatures indicates that initial fission of the B–B bond and then addition is unlikely; more probably, the first stage is π-donation [4] from the olefin into the two vacant *p*-type orbitals of the boron atoms, and these being on adjacent bonded atoms constitute, in effect, a " vacant π-orbital." This would give a π-complex (I) which might either dissociate again or suffer fission of the B–B bond to give the structure (II), as found with ethylene (R =



(I) (II)

R′ = H). The stability of the complex (I) with respect to dissociation into the reactants may be decreased (*a*) if there is repulsion or steric interference between the substituents, R and R′, and the chlorine atoms, and (*b*) if the π-donating ability of the olefin is reduced by the inductive or mesomeric effects of R or R′, either because of decreased electron density at the π-bond or because the latter is made asymmetrical when R ≠ R′. The available evidence suggests that substituent effects are not critical when R = alkyl, but are important when R = halogen; stabilisation against decomposition in the latter case has, however, to be explained. We have therefore investigated the reaction of diboron tetrachloride with trichloroethylene, isobutene, and *cis*- and *trans*-but-2-ene; if double-bond character is lost [*i.e.*, if the adduct (II) is formed], these two isomers should give the same product.

Trichloroethylene and diboron tetrachloride when mixed at −196° and warmed to −78° showed no evidence of solid adduct formation, and after several hours at 20° no reaction could be observed; but the expected rapid decomposition of diboron tetrachloride at this temperature did not occur. Fractionation of the mixture was impracticable, and excess of ammonia was therefore added; this reacts with diboron tetrachloride [5] and would also be expected to react with any stable olefin adduct without liberation of the free olefin.[1] A white solid was obtained, but all the trichloroethylene added was recovered, suggesting that a stable adduct had not been formed. However the ^1H nuclear magnetic resonance spectrum of the diboron tetrachloride–trichloroethylene mixture indicated that two-thirds of the latter had formed a substituted ethane and the remainder had formed an intermediate compound still retaining the double bond. Evidence for the substituted ethane was a multiplet absorption of chemical shift ~183 c./sec. consisting of at least seven bands (all chemical shifts reported here are relative to water as external standard, positive values to the high-field side of the water band). This is consistent with the presence of two rotational isomers each containing a differently shielded hydrogen nucleus interacting with the boron magnetic nucleus ($I = \frac{3}{2}$) to give the observed fine structure. The remainder of the spectrum consisted of a single absorption in the olefinic region of chemical shift −59 c/sec. which could arise from an intermediate of type (I). Formation of either (I) or (II) would explain the observed stabilisation of the diboron tetrachloride; decomposition of the latter to $(BCl)_n$ and boron trichloride might occur by fission of the B–B bond, preceded by internal co-ordination (III), which would be prevented by filling of the vacant boron orbitals (hence the stability of, *e.g.*, the compound $B_2Cl_4,2NMe_3$).

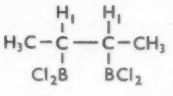
In the reaction of isobutene and diboron tetrachloride, rapid polymerisation of the isobutene occurred; although variable amounts of diboron tetrachloride appeared to have reacted, no adduct was isolated.

Either *cis*- or *trans*-but-2-ene reacted readily with diboron tetrachloride at −78° to give a 1 : 1 addition compound; the reactions were completed in each case by repeated addition

[4] Holliday and Massey, *J. Inorg. Nuclear Chem.*, 1960, in the press.
[5] Urry, Wartik, Moore, and Schlesinger, *J. Amer. Chem. Soc.*, 1954, **76**, 5293.

and removal of the butene, a procedure necessary in the case of the ethylene compound [2] to ensure complete reaction, and the only likely impurity, boron trichloride, was removed in this procedure. From either butene, the addition compound appeared as white crystals at −78°, and the chemical properties were identical, resembling those of the ethylene adduct. Thus, 1 mol. of either reacted with 2 mols. of trimethylamine to give a white

(III)



(IV)

solid which was thermally stable and not readily oxidised or hydrolysed, indicating the probable structure $Me_3N{\cdot}BCl_2{\cdot}CHMe{\cdot}CHMe{\cdot}BCl_2{\cdot}NMe_3$. 2 Mols. of hydrogen chloride added to this compound at room temperature—the corresponding reaction with the ethylene compound was complete only after heating. The addition did not liberate diboron tetrachloride–butene or other volatile products, and the product can be formulated as $[Me_3NH]_2[Cl_3B{\cdot}CHMe{\cdot}CHMe{\cdot}BCl_3]$. As with the ethylene compound, 1 mol. of the butene adduct reacted with 6 mols. of ammonia

$$nB_2Cl_4,C_4H_8 + 6nNH_3 \longrightarrow 4nNH_4Cl + [(BNH)_2,C_4H_6]_n$$

and the required amount of ammonium chloride was separated by sublimation from the other polymeric product. Reaction of either butene adduct with water or alkali at temperatures up to 100° did not give volatile products; *i.e.*, only the B–Cl bonds were attacked:

$$B_2Cl_4,C_4H_8 + 4H_2O \longrightarrow B_2(OH)_4,C_4H_8 + 4HCl$$

The product, like the corresponding ethylene compound, showed acid properties, enhanced by addition of mannitol. Neither butene adduct gave any reaction with ethylene; *i.e.*, the butene was not displaced.

The only observed reaction of diboron tetrachloride–ethylene which gives the free olefin is the oxidation by molecular oxygen, a reaction which is vigorous even at low temperatures.[1] A similar reaction with the butene adducts, releasing either *cis*- or *trans*-but-2-ene, might have helped in the elucidation of the reaction mechanism. Although, as before, oxygen did react with the butene adducts in a 1 : 1 ratio, the reaction was much less vigorous and either a long reaction time or heating was required to complete it. No free olefin was formed; the main product was hydrogen chloride, and a non-volatile polymer remained, in which most of the boron and chlorine were titratable on hydrolysis. A small amount of 2-chlorobutane was found; this could have been formed by reaction of any liberated but-2-ene and hydrogen chloride, and experiment showed that this reaction was catalysed by boron trichloride in presence of oxygen.

These reactions suggest that the butene adducts are identical, with no remaining double-bond character; *i.e.*, both have structure (II), like the ethylene adduct. The infrared spectra of the two butene adducts were identical, and both gave vapour-pressure values close to those reported for B_2Cl_4,C_4H_8 by Schlesinger *et al.*[3] But even after repeated fractionation (with no further change in the spectra), neither adduct melted sharply at the reported [3] temperature of −44·8°. Each preparation gave a product melting over a somewhat different temperature range; *e.g.*, the *cis*-adduct gave m. p. −19° to −22°; −42° to −48°, and the *trans*-adduct −56° to −60°; −25° to −62°. It was not possible therefore to correlate melting range with the particular isomer used.

In order to investigate these peculiarities further, and to confirm the ethane-type structure, the nuclear magnetic resonance spectra of various samples were examined. The ^1H spectra at 40·00 mc./sec. possessed no bands for olefinic-linked hydrogen, indicating that the double bond had been opened. Some of the high-field bands in the spectra of different samples differed in both chemical shift and intensity. However, a broad band at ~120 c./sec. was common to all the spectra and this was assigned to the single hydrogen

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atoms H_1 marked in formula (IV). The intensity of this band was lower than expected but it could be assigned with confidence since the hydrogen-1 spectrum of diboron tetrachloride–ethylene has a similar band, of this chemical shift and possessing no spin–spin interaction fine structure from the boron-11 nucleus. Such splittings are therefore assumed to be absent from the spectra of the butene adducts. The remaining bands of the spectrum corresponded to methyl-type hydrogen and in some cases extended over the range 145—183 c./sec. At 16·2 mc./sec. the spectra of some samples possessed at least four chemical shifts in the methyl region of the spectrum. None of these could be due to *cis*- or *trans*-butene impurities since there was no olefinic-linked hydrogen present, and the high-field bands of the but-2-ene compounds would also be readily recognisable. A freely rotating ethane-type structure would have resulted in a spectrum with a quartet for the lone hydrogen atoms and a doublet for the methyl groups with only two chemical shifts involved. Hindered rotation about the central C–C bond could give rise to three differently shielded methyl groups: further hindered rotation of the methyl groups themselves would result in a spectrum having more than three chemical shifts in the methyl region. Further evidence that this situation prevails is provided by the broad nature of the band of the lone hydrogen atoms. An examination of models of these compounds indicated that hindered rotation is possible; any remaining double-bond character would of course make it more likely. The varying intensities of some of the bands in the methyl region resulted from the presence of different amounts of the various rotational isomers in the different samples, and this would explain the melting-point peculiarities. The absence of an equilibrium mixture indicates that the populations of the isomers were controlled by some factor in their preparation and that, once formed, the energy barriers separating them were high enough to prevent interconversion at room temperature. This was further confirmed by examining the samples over the range −60° to +60°, no marked change in the spectra being observed.

Had the spectra of the *cis*- and *trans*-compounds been consistently different owing to the non-equivalence of the hydrogen atoms in hindered-rotation *meso*- and racemic forms,[6] it would have been possible to confirm that the diboron tetrachloride does not dissociate before addition of the olefin, and correlation with the expected isomers, diboron tetrachloride being assumed to be planar, would be further evidence for this structure.

Experimental

The preparation of diboron tetrachloride, and the methods used to study its reactions, have been described previously.[1] Trichloroethylene was dried (Na_2SO_4) and fractionated; it had v. p. 21 mm. at 0°. Pure samples of *cis*- and *trans*-but-2-ene were obtained from the National Chemical Laboratory. ^1H high-resolution nuclear magnetic resonance spectra were obtained at 40·00 mc./sec. by use of a Varian V-4300B spectrometer equipped with a field stabiliser.

In the following experiments, units are mmoles or mg.-atoms unless otherwise stated.

Reactions of Diboron Tetrachloride.—(i) *With trichloroethylene.* Diboron tetrachloride (1·44) and trichloroethylene (1·17) when warmed from −196° gave no solid product at −78°. After warming to 20° for 1 hr., excess of ammonia was added to give a white solid; trichloroethylene (1·17) was the only volatile product.

(ii) *With* cis- *or* trans-*but-2-ene.* In a typical experiment, *cis*-but-2-ene (2·12) was condensed on diboron tetrachloride (1·72), and the mixture warmed to −78°. Material volatile at this temperature was distilled off and returned to the reaction vessel several times, and finally the mixture was stored for ~18 hr. at −78°. The solid *product* then weighed 0·388 g. (= 1·76 of $B_2Cl_4.C_4H_8$) and *cis*-but-2-ene (0·42) was recovered. Hydrolysis of the product with excess of sodium hydroxide for 1 hr. at 100° gave Cl, 7·02 ($B_2Cl_4.C_4H_8$ requires Cl, 7·04); no butene was recovered.

Reactions of the But-2-ene Adducts with Trimethylamine and Ammonia.—In a typical experiment, excess of trimethylamine (2·76) was condensed on the adduct (0·97) at −196°; on warming, a vigorous reaction followed melting of the reactants. Trimethylamine (1·53) was recovered

[6] Lee and Sutcliffe, *Trans. Faraday Soc.*, 1959, **55**, 880.

after 18 hr. at 20° and returned to the reaction vessel; after 1 minute's heating at 50°, trimethylamine (0·75) was recovered. The solid *product* weighed 0·339 g. (= 1·00 of $B_2Cl_4,C_4H_8,2NMe_3$); hydrolysis with boiling sodium hydroxide solution gave Cl, 3·90 ($B_2Cl_4,C_4H_8,2NMe_3$ requires Cl, 4·00). Treatment of the product with excess of methyl alcohol or water at 20° gave quantitative recovery of these reagents, but when the product (1·00) was treated with hydrogen chloride (3·60) at 20°, recovery of hydrogen chloride was 1·74, with no further uptake on heating, and no other volatile product; hydrolysis of the solid *product* gave Cl, 5·7 ($B_2Cl_4,C_4H_8,2NMe_3,2HCl$ requires Cl, 6·00).

Excess of ammonia (2·46) was condensed on the adduct B_2Cl_4,C_4H_8 (0·205), and the mixture warmed to 20°. After the vigorous reaction, ammonia (1·25) was recovered, but no other volatile product. The solid residue on heating gave a sublimate of ammonium chloride (0·80), leaving a white solid product. Hence reaction ratio, adduct : NH_3 used : NH_4Cl = 1 : 5·9 : 3·9.

Oxidation of the But-2-ene Adducts.—The reactions were carried out as previously described; [1] details are tabulated:

Time (hr.) and temp.	6 at 20°	125 at 20°, 0·25 at 50°	2 at 80°, 200 at 20°
B_2Cl_4,C_4H_8 used	0·28	0·50	0·62
O_2 used	0·21	0·51	0·63
Products: HCl	0·39	0·81	1·01
BCl_3	0·13	0·03	0·00
C_4H_9Cl	0·10	0·09	0·18
Residue: Cl^- (titrn.)	0·12	0·45	0·67
B (titrn.)	0·34	0·91	1·04

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64. *Diffusional Band Spreading in Gas-chromatographic Columns. Part I. The Elution of Unsorbed Gases.*

By J. Bohemen and J. H. Purnell.

It has been shown that diffusion coefficients can be measured reasonably accurately from elution curves, and that the labyrinth constant for packed columns, γ, is probably unity. The eddy diffusion contribution to the plate height cannot be measured reliably, but probably lies between one and two support-particle diameters.

The rate theory of chromatography as presented by van Deemter, Zuiderweg, and Klinkenberg [1] has formed the basis of most studies of column performance. In its simplest form their equation reads

$$H = A + B/u + Cu \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where H is the height equivalent to a theoretical plate, u is the carrier-fluid velocity, $A = 2\lambda d_p$, λ being an eddy diffusion constant, and d_p the support-particle diameter, $B = 2\gamma D_g$; γ is called the labyrinth factor, and D_g is the interdiffusion coefficient of the solute in the mobile (gas) phase; C is a coefficient relating to the rate of mass transfer in the sorbent phase.

In several investigations carried out to test this equation, the results generally fit an equation of this type, but the individual terms are rarely concordant. For example, some of the earlier results [1,2] indicated that λ increased with decreasing particle diameter, being as high as 8 for a column packed with Celite of $d_p \sim 30$ μ. Glueckauf,[4] however, found λ

[1] van Deemter, Zuiderweg, and Klinkenberg, *Chem. Eng. Sci.*, 1956, **5**, 271.
[2] Keulemans and Kwantes, in " Vapour Phase Chromatography (report of symposium), 1957," ed. Desty, Butterworths, London, p. 15.
[3] Desty, Godfrey, and Harbourn, in " Gas Chromatography (report of symposium), 1958," ed. Desty, Butterworths, London, p. 200.
[4] Glueckauf, in ref. 3, p. 33.

to be about unity, and values between 0·3 and 1·5 may be inferred from other work.[3-6] It has also been suggested [5,7,8] that λ may be zero or effectively so. Values obtained for B indicate [1-5,7,9] that γ lies between about 0·5 and 1, and the present authors [5] found evidence which suggested that $B = k_1 + k_2 d_p$, k_1 and k_2 being constants. The apparent conflict seems most likely to arise from inaccuracies in the determination of H, incorrect interpretation and evaluation of u, the use of insufficiently wide ranges of velocities, the use of graphical methods in the calculation of A, B, and C, and, finally, the approximate nature of equation (1). In the work described here every effort has been made to eliminate errors arising from these sources. The experiments designed to evaluate λ and γ involved a comparison of the elution of unsorbed gases from both open tubes and packed columns. Further, cognisance was taken of the need to introduce a coefficient C_g relating to mass-transfer effects in the gas phase as indicated by Golay [10] and van Deemter,[11] and also that B and C_g were pressure-dependent. Extending equation (1) we have

$$H = A + B/u + (C_g + C_l)u \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where C_l is the liquid mass-transfer coefficient. The appropriate velocity is that corrected for the compressibility of the carrier gas by use of James and Martin's correction factor f; [12] thus $u = u_0 f$, where u_0 is the carrier-gas velocity measured at the column outlet pressure. However, it has been shown [8] that $B = B_0 f$, and because of the inverse relation of C_g to D_g, presumably, $C_g = C_g^0/f$, B_0 and C_g^0 being values again corresponding to the outlet pressure. In order to standardise B and C, they may be converted into their values at 1 atm. pressure, B' and C_g', and then

$$H = A + B'/p_0 u_0 + C_g' p_0 u_0 + C_l u_0 f \quad . \quad . \quad . \quad . \quad . \quad (3)$$

p_0 being the column outlet pressure (in atm.). However, $p_0 u_0 = u'$, the gas velocity corresponding to unit outlet pressure, hence

$$H = A + B'/u' + C_g' u' + C_l u' f/p_0 \quad . \quad . \quad . \quad . \quad . \quad (4)$$

For our present purposes, since the work is associated with the elution of unsorbed materials, the last term vanishes and the relevant equation for further discussion is

$$H = A + B'/u' + C_g' u' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Experimental

Gas samples were added to the carrier-gas stream by means of the stainless-steel rotary valve described below. They then passed through one side of a twin-cell katharometer before entering the chromatographic column. Thus, an " injection peak " was recorded and so both the initial volume occupied by the sample and the time of sample introduction could be accurately determined. The other cell of the katharometer was used to monitor the column effluent. The carrier gas was oxygen-free nitrogen from a cylinder. Throughout the experiments the columns were kept at 51° in a forced-convection air-thermostat.

Sample-injection System.—Many methods of and devices for injecting samples into the carrier-gas stream were tried, but were all found to be unsatisfactory for the projected experiments. So a new type was devised (see Fig. 1). The multiple on-off, isolating action derives

[5] Bohemen and Purnell, in ref. 3, p. 6.
[6] Scott, in ref. 3, p. 189.
[7] Littlewood, in ref. 3, p. 23.
[8] Brennan and Kemball, *J. Inst. Petroleum*, 1958, **44**, 14.
[9] Rijnders, in ref. 3, p. 18.
[10] Golay, in ref. 3, p. 36.
[11] van Deemter, Informal Symposium, Gas Chromatography Discussion Group, Cambridge, Oct. 4th, 1957.
[12] James and Martin, *Biochem. J.*, 1952, **50**, 679.

from a set of sloping O rings. With the valve in the position shown in the diagram the carrier gas entered port 1, went through the valve between barrel and key, and then left by port 2, which was connected to the katharometer with 1·4 mm. internal-diameter stainless-steel tubing. A 1 ml. volume stainless-steel by-pass, to which a modified petrol union containing a serum cap was hard-soldered so as to enable syringe injection of samples, was connected across ports 3 and 4. All connections to the ports of the rotary valve were made by means of the O ring connector also illustrated in Fig. 1. Samples of the permanent gases after introduction into the by-pass were then swept into the carrier-gas stream by rotating the inner cylinder of the valve through 180°.

Construction of Columns.—Columns were packed in stainless-steel tubing of measured length and diameter, the columns, in each case, being packed after the tubes had been bent into a U-shape. All the columns containing Sil-O-Cel firebrick contained also polyethylene glycol 400, which had been distributed on the brick by deposition from a solution in acetone.

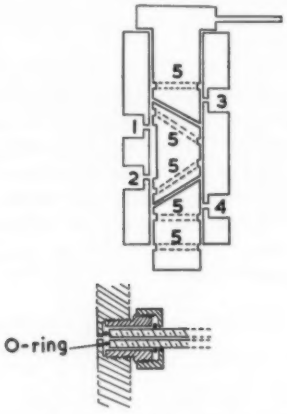

FIG. 1. *Sampling valve and* O *ring connectors.*
1, *Carrier-gas entry*; 2, *outlet to column*; 3 *and* 4, *by-pass volume*; 5, *isolating* O *rings.*

The prepared material, after being heated under a vacuum, was poured into the stainless-steel tube and packed down by tapping the column. Initially, the decrease in the volume occupied by the packing was rapid but, after about 10 min., the rate of volume change became substantially constant. Study revealed that this steady decrease was due to break-up of the solid particles, and hence the packing procedure was discontinued when this stage was reached.

The long columns containing glass beads were packed by passing nitrogen through the column and tapping as before. The packing density was found to be practically independent of the column length.

Determination of Column Efficiencies.—The number of theoretical plates, N, associated with any solute eluted from a column was determined by use of Glueckauf's equation [13] $N = 8(l/w_e)^2$ where w_e is the width of the elution curve at the $(1/e)$th height and l is the distance between the point of injection and the peak maximum. The method of evaluating N which was suggested at the 1956 London Symposium was not adopted, since it was impossible to draw tangents at the points of inflection of narrow elution curves accurately.

The moment of sample injection was accurately known from the " injection " peak. When peaks emerged rapidly from the column the chart speed was increased suitably; the maximum speed available with the 1 mv Honeywell–Brown recorder used in this work was 120″ per hour. The chart speed was checked at frequent intervals and was found to be constant although about ½% less than was specified. l and w_e were generally measured with a travelling microscope.

RESULTS AND DISCUSSION

Permeability to Gas Flow.—The measurement of column permeability provides an independent method for determining the mean size of the particles of packing. The gas

[13] Glueckauf, *Trans. Faraday Soc.*, 1955, **51**, 34.

velocity at the column outlet, u_0, defined by $u_0 = F_0/A\varepsilon$, where F_0 is the volume flow rate measured at the column temperature and outlet p_0, A is the cross-sectional area of the containing tube, and ε is the porosity, is related to column parameters by $u_0 = B_0(p_i^2 - p_0^2)/2\eta\varepsilon L p_0$, p_i being the column inlet pressure, L the column length, η the viscosity coefficient, and B_0 the specific permeability coefficient. By plotting u_0 against $[(p_i^2 - p_0^2)/p_0]$, B_0 can be evaluated if L, η, and ε are known or measured. The value of η used here ($1{\cdot}91 \times 10^{-4}$ g. cm.$^{-1}$ sec.$^{-1}$) was calculated from the equation quoted by Moelwyn-Hughes,[14] while ε was measured by use of the equation $\varepsilon = 1 - m\rho_b/V_c$, wherein, for Sil-O-Cel, ρ_b is the particle density measured under mercury (bulk density), while for glass beads it represents the true density; m is the mass of packing and V_c is the total packed column volume.

According to the Kozeny–Carman equation [15]

$$B_0 = d_p^2\varepsilon^3/180(1 - \varepsilon)^2$$

where d_p is the diameter of a sphere with the same specific surface as the particles in the bed. Some values of ε and of d_p derived from evaluations of B_0 for some firebrick and glass bead columns are listed in Table 1. Included for the former are surface areas per gram of solid, S, calculated from $S = 0{\cdot}75(1 - \varepsilon)V_c/d_p$, values of d_p derived from B_0 again being used.

TABLE 1.

Firebrick

Column	Length (cm.)	Sieve size (range) (mm.)	ε	d_p (mm.	Surface area (cm.^{2} g.$^{-1}$)
1	136	0·635—0·425	0·465	0·32	258
2	131	0·254—0·211	0·444	0·16	516
3	120	0·127—0·084	0·391	0·10	825

Glass beads

Column	Length (cm.)	Manufacturer's quoted size (mm.)	ε	d_p (mm.
4	100	0·11	0·377	0·088
5	99	0·10	0·359	0·080
6	376	0·10	0·365	0·079
7	378	0·3—0·4	0·370	0·376

The derived values of d_p for the glass-bead columns 4 and 5 are somewhat lower than the manufacturer's quotation, but are in the same ratio. Columns 5 and 6, constructed of the same beads, differed considerably in length but gave the same result for d_p while 6 and 7, constructed of beads of different diameter, operated under pressure gradients differing by a factor of nearly twenty. The results obtained are, therefore, sufficiently good to substantiate the experimental procedure employed and to validate the extension of the method to the Sil-O-Cel columns. The considerable discrepancy between the listed values of d_p and the sieve grades for the coarser Sil-O-Cel particles can, therefore, be taken to show that sieve sizes are unreliable as a means of determining d_p. In any event, the particle diameter used in the original derivation of equation (1) was that defined by the permeability equation, and so is the one appropriate to the discussion of the dependence of the column efficiency on support particle size.

The results listed in Table 1 for the Sil-O-Cel columns show conclusively that resistance to gas flow arises from the external surface of the particles only. The largest Sil-O-Cel surface area measured, *e.g.*, that for column 3, is only 825 cm.^{2} g.$^{-1}$, in contrast to the value of 3×10^4 cm.^{2} g.$^{-1}$ found from adsorption measurements.[16] These and the earlier results show that the Kozeny–Carman equation is applicable to the flow of gas through

[14] Moelwyn-Hughes, "Physical Chemistry," Pergamon Press, London, p. 597.
[15] Carman, "The Flow of Gases through Porous Media," Butterworths, London, p. 8.
[16] Bohemen, Langer, Perrett, and Purnell, *J.*, 1960, 2444.

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chromatographic columns, and also that this flow does not involve the internal volume of the particles.

Retention Volume of Unsorbed Gases.—The retention volume, V_d, of hydrogen and carbon dioxide eluted in nitrogen from columns 1—7 are listed in Table 2, which includes also the interparticle (void) volumes V_v, the intraparticle (pore) volumns V_p, and their sums. The retention volumes were measured integrally and each is the mean of 25—50 measurements. The results in the Table represent altogether more than 300 measurements.

TABLE 2.

Column	V_p	V_v	$(V_p + V_v)$	V_d (H_2)	V_d (CO_2)	Column	V_p	V_v	$(V_p + V_v)$	V_d (H_2)	V_d (CO_2)
1	5·5	9·6	15·1	16·1	18·0	4	—	5·7	5·7	5·8	—
2	5·5	8·7	14·2	15·0	17·0	5	—	5·4	5·4	5·7	—
3	5·5	7·0	12·5	13·8	15·7	6	—	21·0	21·0	21·4	—
						7	—	21·4	21·4	21·8	—

As would be expected, the retention volume of hydrogen eluted from glass-bead columns corresponds closely to the void volume. With Sil-O-Cel columns, however, the retention volumes are about twice the void volume and close to the sum $(V_v + V_p)$, that is, the total column free-gas volume. Similar findings have been described by Primavesi.[17] The slight discrepancies are greater than the errors involved in the measurements and so are probably due to unavoidable sorption, a view which is supported by the greater retention of carbon dioxide than of hydrogen. Since it has already been shown that carrier-gas flow occurs between the particles only, the equivalence of V_d and $(V_p + V_v)$ requires explanation. This is as follows.

Consider a single theoretical plate in a column containing only a porous non-sorbing solid. The total gas space is divided into a mobile volume ΔV_v and a static volume ΔV_p. If a sample of some gas is injected into the static carrier gas already in this plate it will be uniformly distributed through both ΔV_v and ΔV_p. Addition to the plate now of a volume ΔV_v of carrier gas carries the original contents of the plate void volume on into the next plate, but leaves the contents of the pore volume behind. The latter then equilibrate throughout the total gas space. Continued addition of carrier thus leads to a partitional spreading of the initial, injected gas packet, and the process is effectively gas–gas chromatography. The necessary "immiscibility" of phases arises from the relative motions of the two gas regions. Thus, the conventional chromatographic retention volume equation can be applied, and $V_d = V_v + KV_p$. However, since gases are miscible in all proportions, the partition coefficient K is always unity, *i.e.*, at equilibrium the concentrations in ΔV_v and ΔV_p are identical, and hence $V_d = V_v + V_p$, as found. That the equilibration process involved is virtually instantaneous follows from the fact that it is ignored in column theory. More important, the process must precede all other partitional mechanisms in packed columns and since the partition coefficients determined by gas–liquid chromatography commonly agree well with those found by static methods, it must therefore occur very rapidly indeed.

These results and the explanation offered are important, since they establish that the retention volume of an unsorbed gas does not measure the void volume alone if the solid support is porous. Thus, it is correct to calculate the capacity factor k of the van Deemter and the Golay theory from the ratio $(V_R' - V_d)/V_d$, where V_R' is the apparent retention volume of some sorbed substance and V_d is that of an unsorbed material. Further, partition coefficients calculated from $(V_R' - V_d) = KV_l$, where V_l is the volume of stationary phase, are not subject to error. However, it is incorrect to calculate carrier-gas velocities for use in theoretical studies from the retention times of unsorbed substances (air). These must be evaluated from volume flow and porosity data. If they are not, then, for example, values of B derived from application of equation (1) to the results will be too small by about a factor of 2, while C will be correspondingly too great. This

[17] Primavesi, Informal Symposium, Gas Chromatography Discussion Group, Bristol, Sept. 25th, 1959.

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might explain some of the low values of γ in the literature. It might be thought that the contribution of a longitudinal diffusional band spreading to the theoretical plate height would be determined by the total time spent in the column, but, in fact, the process only contributes to H during the time spent by the material in the void volume because d_p must, according to theory, be smaller than H. Thus, within the particle there must be uniformity of concentration, and spreading from plate to plate can only occur in the void volume.

Diffusion Coefficients from Elution Data for Open Tubes.—For elution from an open tube, equation (5) reduces to

$$H = 2D_g'/u' + C_g'u' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

In the conditions of the present experiments the contribution of the second term in (6) to the value of H never exceeded 3%, hence, to a reasonable approximation,

$$H = 2D_g'/u' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Table 3 lists values of D_g' derived through equation (7) and also the corresponding literature values for hydrogen,[18] oxygen,[18] and carbon dioxide [19] in nitrogen at 51°. Also included for the last two are D_g' values deduced through (6), which show that C_g' may, in fact, be neglected in subsequent discussion. The appropriate values of C_g' were calculated from Golay's equation [10] $C_g' = r_0^2/24D_g'$, wherein r_0 is the tube radius.

TABLE 3. *Interdiffusion coefficients: some permanent gases in nitrogen at* 1 *atm. pressure and* 51°.

Gas	u' (cm. sec.$^{-1}$)	D_g' (cm.^{2} sec.$^{-1}$)	D_g' (6) (cm.^{2} sec.$^{-1}$)	D_g' (lit.) (cm.^{2} sec.$^{-1}$)
Hydrogen	0·85	0·876	—	
	1·28	0·881	—	0·909
	1·56	0·919	—	
Oxygen	0·72	0·260	0·258	0·244
	1·42	0·267	0·261	
Carbon dioxide	0·73	0·188	0·186	0·194

The agreement between the chromatographic values and those in the literature is good, the greatest discrepancy being about 7%. The chromatographic values increase slightly with increased velocity, a feature which to some extent, but not completely, is remedied by use of equation (6). The method is evidently suited to the determination of diffusion coefficients, and the findings provide a basis for the extension of equation (6) to packed columns.

Diffusion Coefficients from Elution Data for Packed Columns.—For unsorbed gases in packed columns operated at low velocity the basic equation (5) reduces to

$$H = A + B'/u' \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

A plot of H against $1/u'$ should be linear, of slope $2\gamma D_g'$ and intercept A. Plots of this type were used by Glueckauf [4] in connection with frontal technique studies. Fig. 2 shows such plots obtained in this work for the elution of both hydrogen and carbon dioxide in nitrogen at 51° from a Sil-O-Cel column of $d_p = 0{\cdot}01$ cm. Both sets of figures give straight lines and the fit of all points, which represent an average of at least three measurements, is excellent. Even so, the intercepts for the two gases differ by 50%. This illustrates the extreme difficulty of evaluating A with any certainty by graphical methods.

An alternative procedure is to evaluate A and B' by a method of successive approximation using equation (8). Values found in this way for columns 1, 2, and 3 and also calculated values of λ and γ are contained in Table 4, representing about 30 measurements with each column extending over the carrier-gas velocity range 1—10 cm. sec.$^{-1}$ for hydrogen and 1—5 cm. sec.$^{-1}$ for carbon dioxide elution. The values of A listed are not

[18] Internat. Critical Tables, Vol. V, p. 62.
[19] Boardman and Wild, *Proc. Roy. Soc.*, 1937, *A*, **162**, 511.

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TABLE 4.

	Hydrogen				Carbon dioxide			
Column	A (cm.)	λ	B' (cm.^{2} sec.$^{-1}$)	$B'/2D_g' = \gamma$	A (cm.)	λ	B' (cm.^{2} sec.$^{-1}$)	$B'/2D_g' = \gamma$
1	0·030	0·5	1·72	0·95	0·039	0·6	0·335	0·86
2	0·025	0·8	1·85	1·02	0·024	0·7	0·380	0·98
3	0·030	1·5	1·75	0·96	0·023	1·2	0·344	0·89

considered to be more accurate than $\pm 0{\cdot}005$, but values of B' are probably good to $\pm 0{\cdot}02$ for hydrogen and $\pm 0{\cdot}01$ for carbon dioxide. The combined values of A and B' in each case reproduce the experimental data to better than 3% over the whole range of velocities.

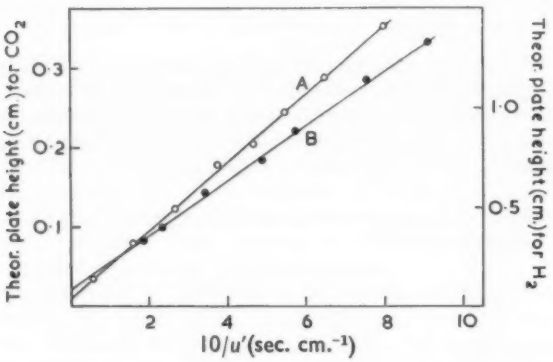

FIG. 2. *Dependence of H upon* $1/u'$ *in the elution of* (A) *hydrogen and* (B) *carbon dioxide in nitrogen at* 51° *from Sil-O-Cel column of* d_p = 0·010 *cm.*

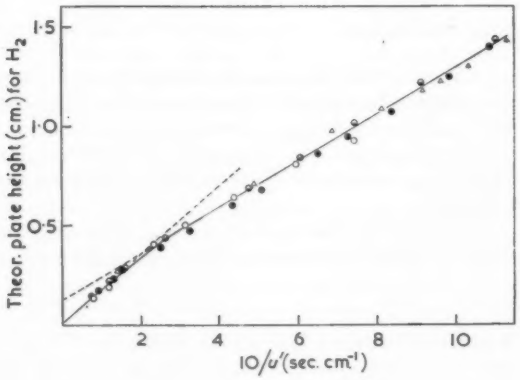

FIG. 3. *Dependence of H upon* $1/u'$ *in the elution of hydrogen in nitrogen at* 51° *from four glass-bead columns. Column nos.:* ○ 4; △ 5; ◒ 6; ● 7.

The values of λ agree reasonably for the two gases and apparently increase with decreasing d_p in such a way as to keep A roughly constant. However, the variation is comparable to the probable accuracy of the measurements, and so λ may be independent of d_p. The only safe conclusion is that λ probably lies between 0·5 and 1.

The average value of γ is 0·94, which is the highest yet recorded and may result from the method used here to calculate the carrier-gas velocity. Had the air peak retention time been used for the latter purpose, a mean γ of 0·60 would have been obtained. There is no obvious trend of γ with changing d_p, although γ is high when A is low. This might mean that the variations in γ are associated with exaggerated estimates of A.

Fig. 3 shows data for the elution of hydrogen in nitrogen, at 51°, from the four columns of glass beads (4—7). The dependence of H upon $1/u'$ is seen to be independent of column

length, and the pressure correction method for the velocity is verified, since the pressure drop across columns 6 and 7, at a given velocity, differed by as much as a factor of 18. In addition, H is virtually independent of d_p, as would be expected if A were very small. An unexpected feature of the results is that in the range $1/u' = 0$—2 sec. cm.$^{-1}$, the derived values of γ agree with those determined for Sil-O-Cel columns. At higher values of $1/u'$, however, γ appears to be about 0·6, in accord with the findings of earlier workers.[4,7] The values of A obtained by extrapolation of the low-velocity data are obviously of little significance since lower values of H are achieved in practice at high velocities. The reason for the change of slope of the graph, which was not observed with the packed columns, is unknown. The effects observed on going towards higher velocities are the opposite of those to be expected if some gas mass-transfer mechanism is operative. It may thus be that the anomaly is associated with localised gas-flow irregularities which depend upon the smoothness or roughness of the particles in the bed.

The conclusions to be drawn from this work are that while B' and, hence, D_g', may be reasonably accurately determined from chromatographic data through the van Deemter equation, it is not possible, even with extreme experimental precautions, to make an unequivocal estimate of the magnitude of A. However, it seems established that λ never significantly exceeds unity, and so eddy diffusion is not, here at least, a limiting factor in the attainment of high column efficiencies.

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Department of Physical Chemistry,
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65. *The Preparation and Oxidation of Sulphides formed from o-Nitrobenzenesulphenyl Chloride and Ketones.*

By I. L. Finar and A. J. Montgomery.

o-Nitrobenzenesulphenyl chloride reacts with acetone, acetophenone, acetylacetone, benzoylacetone, and dibenzoylmethane to form sulphides (I—V). Oxidation with hydrogen peroxide at 80° converts both sulphides (I) and (III) into sulphone (VI), and both (II) and (IV) into sulphone (VII). Oxidation at room temperature again produces (VI) from both (I) and (III), but (IV) and (V) give the corresponding sulphoxides (VIII) and (IX). Some properties of the sulphoxides have been examined and reductions have been carried out on the sulphides.

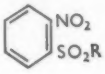
o-Nitrobenzenesulphenyl chloride reacts with acetone,[1] acetophenone,[2] acetylacetone, benzoylacetone, and dibenzoylmethane to form respectively the sulphides (I—V). The sulphides (III, IV, and V) were also prepared by reaction of the sulphenyl chloride with the copper complex of the corresponding diketone. When these sulphides were oxidised with hydrogen peroxide in acetic acid–acetic anhydride [3] at 80°, the acetyl compound (I) and (III) gave the sulphone (VI), the sulphides (II) and (IV) gave the sulphone (VII), and the dibenzoyl compound (V) gave benzoic acid. When the oxidation was carried out at 20°, (I) and (III) again gave the sulphone (VI), but (IV) now gave the sulphoxide (VIII), and (V) gave the sulphoxide (IX). The sulphoxides (VIII and IX) were unstable to heat and easily hydrolysed by dilute acid in ethanol to benzoylacetone and dibenzoylmethane, respectively. The sulphoxide (VIII), when refluxed with aqueous ammonia or dilute

[1] Zincke and Farr, *Annalen*, 1912, **391**, 57.
[2] Kharasch, Wehrmeister, and Zigermann, *J. Amer. Chem. Soc.*, 1947, **69**, 1613.
[3] Truitt, Stead, and Long, *J. Amer. Chem. Soc.*, 1949, **71**, 3511.

aqueous ethanol, gave the simpler sulphoxide (X). Sulphoxides (VIII) and (X) were oxidised to the same sulphone (VII) by hydrogen peroxide.

Reduction of the sulphides (III, IV, and V) with stannous chloride in acetic acid containing hydrogen chloride (cf. Zincke and Baeumer [4]) produced 2-methylbenzothiazole

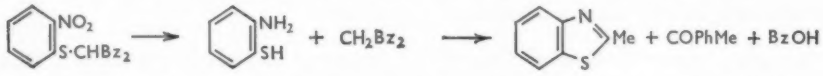
(I) R = CH_2Ac
(II) R = CH_2Bz
(III) R = $CHAc_2$
(IV) R = CHBzAc
(V) R = $CHBz_2$



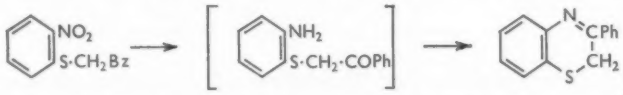
(VI) R = CH_2Ac
(VII) R = CH_2Bz

(VIII) R = CHBzAc
(IX) R = $CHBz_2$
(X) R = CH_2Bz

as one of the products. This reaction probably proceeds by scission of the S–C bond, resulting in the intermediate formation of the diketone and thiophenol, the latter then reacting with the solvent (acetic acid) to form 2-methylbenzothiazole, *e.g.*, with (V):



This is supported by the fact that dibenzoylmethane, when treated under the same conditions with the stannous chloride solution, gave acetophenone and benzoic acid.



On the other hand, reduction of the sulphide (II) produced 3-phenyl-1,4-benzothiazine [5] by ring closure of the intermediate amino-sulphide.

Experimental

Reaction of o-Nitrobenzenesulphenyl Chloride with Ketones and Diketones.—(*a*) A solution of *o*-nitrobenzenesulphenyl chloride (7·6 g., 0·04 mole) and acetophenone (6 g., 0·05 mole) in ethylene chloride (100 c.c.) was refluxed until hydrogen chloride was no longer evolved (4 hr.). The solution was stored for 2—3 hr., and the solid which separated was collected, dried, and recrystallised from chloroform–hexane to give yellow plates of ω-(*o*-nitrophenylthio)acetophenone (II), m. p. 145—146° (80%) (Kharasch *et al.*[2] give m. p. 141°). Reaction of the sulphenyl chloride with acetylacetone, benzoylacetone, and dibenzoylmethane was carried out as above (see Table). With acetone, only 1·5 hours' heating was necessary, and the excess of acetone was distilled off.

Sulphide	M. p.*	Yield (%)	Found (%) C	H	N	S	Formula	Required (%) C	H	N	S
(I)	81—82° [a]	75									
(II)	145—146 [b]	60									
(III)	141·5—142·5 [a]	70	52·3	4·3	5·5	12·4	$C_{11}H_{11}NO_4S$	52·2	4·35	5·5	12·65
(IV)	116·5—117·5 [c]	65	61·0	4·15	4·1	9·9	$C_{16}H_{13}NO_4S$	60·95	4·1	4·4	10·2
(V)	149—149·5 [c]	55	67·0	3·9	3·4	8·4	$C_{21}H_{15}NO_4S$	66·8	4·0	3·7	8·5

* Solvents for recrystallisation: (*a*) aqueous ethanol, (*b*) chloroform–hexane, (*c*) aqueous acetic acid.

(*b*) A solution of the sulphenyl chloride (0·02 mole) and the copper complex (0·01 mole) of acetylacetone, benzoylacetone, or dibenzoylmethane in dry chloroform was refluxed for 15 min.,

[4] Zincke and Baeumer, *Annalen*, 1918, **416**, 108.
[5] Unger, *Ber.*, 1897, **30**, 609.

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filtered, and washed with dilute sulphuric acid, then water, and dried (Na_2SO_4). The chloroform was distilled off, and the residue recrystallised to give the required sulphides. The yields in these cases were 62—70%.

Oxidation of Sulphides.[3]—(a) The sulphide (4 g.) was suspended in glacial acetic acid (40 c.c.) and acetic anhydride (10 c.c.), and the mixture heated to 80°. Hydrogen peroxide (30%; 10 c.c.) was then added dropwise at such a rate that the temperature remained at 70—80° during the addition. The solution was then heated on a steam-bath for 15 min. and allowed to cool. For isolation of sulphone (VI) the solution was diluted with water and extracted with ether, the ether washed and evaporated, and the residue crystallised from aqueous ethanol. Sulphone (VII) was precipitated when the solution was set aside, and was also recrystallised from aqueous ethanol. Sulphide (I) gave *acetonyl o-nitrophenyl sulphone* (VI) (45%), m. p. 84—85° (Found: S, 12·9. $C_9H_9NO_5S$ requires S, 13·2%); (II) gave *phenacyl o-nitrophenyl sulphone* (VII) (80%), m. p. 136·5—137·5° (Found: S, 10·2. $C_{14}H_{11}NO_5S$ requires S, 10·5%); (III) gave (VI; 25%); (IV) gave (VII; 30%); only benzoic acid (60%) was isolated from (V).

(b) *Oxidations at* 20°. A mixture of the sulphide (4 g.), acetic acid (40 c.c.), acetic anhydride (10 c.c.), and 30% hydrogen peroxide (10 c.c.) was stored for 5 days at 15—20°. Sulphides (I) and (III) each gave sulphone (VI) (35%), extracted with ether after dilution with water (as above); (II) gave sulphone (VII) (80%) as a precipitate; (IV) gave *α-acetylphenacyl o-nitrophenyl sulphoxide* (VIII) (70%) as a precipitate which when washed with water and dried had m. p. 107—108° (decomp.) (Found: C, 57·7; H, 3·7; N, 4·5; S, 10·0. $C_{16}H_{13}NO_5S$ requires C, 58·0; H, 3·9; N, 4·2; S, 9·7%); (V) gave *dibenzoylmethyl o-nitrophenyl sulphoxide* (IX) (96%) as a precipitate which when washed with water, ethanol, and ether, had m. p. 103·5—104° (Found: C, 63·9; H, 3·6; N, 3·5; S, 7·9. $C_{21}H_{15}NO_5S$ requires C, 64·1; H, 3·8; N, 3·6; S, 8·1%).

Hydrolysis of Diketo-sulphoxides (VIII) *and* (IX).—The sulphoxide (3 g.) was suspended in 95% ethanol (50 c.c.), dilute hydrochloric acid (15 c.c.) added, and the mixture heated on a steam-bath until a clear solution resulted (1·5 hr.). The solution was cooled and diluted with water, and the precipitate collected, dried, and recrystallised; (VIII) gave benzoylacetone (77%), and (IX) gave dibenzoylmethane (70%).

Preparation of o-Nitrophenyl Phenacyl Sulphoxide (X).—The sulphoxide (VIII) (2 g.) was heated on a steam-bath with dilute aqueous ammonia for 20 min., and the mixture allowed to cool and then filtered. The residue was washed with dilute sulphuric acid and recrystallised from ethanol to give *o-nitrophenyl phenacyl sulphoxide* (X), m. p. 148—149° (decomp.) (Found: S, 11·0. $C_{14}H_{11}NO_4S$ requires S, 11·1%). A further crop was obtained by acidification of the mother-liquor, the total yield being 97%.

Oxidation of Sulphoxides.—A solution of sulphoxide (X) (2·9 g.) in acetic acid (40 c.c.) and 30% hydrogen peroxide (5 c.c.) was heated on the steam-bath for 30 min., allowed to cool, and diluted with water, and the precipitate recrystallised from aqueous ethanol to give the sulphone (VII) (60%).

A suspension of sulphoxide (VIII) (3 g.) in acetic acid (30 c.c.) and acetic anhydride (7·5 c.c.) was heated to 80°, and 30% hydrogen peroxide (7·5 c.c.) added dropwise. The solution was cooled and diluted with water, and the precipitate recrystallised from aqueous ethanol to give the sulphone (VII) (50%).

Reduction of the Nitro-sulphides.—Stannous chloride solution [4] was prepared by bubbling dry hydrogen chloride through a suspension of stannous chloride (200 g.) in acetic acid (380 c.c.) until a clear solution was obtained. A mixture of nitro-sulphide (5 g.) and stannous chloride solution (50 c.c.) was refluxed for 4—6 hr., cooled, and made just alkaline with 10% aqueous sodium hydroxide.

(a) *Sulphide* (II). The alkaline solution was extracted with nitrobenzene (3 × 100 c.c.), the extract steam-distilled, and the residue recrystallised from nitrobenzene–ethanol to give 3-phenyl-1,4-benzothiazine (40%), m. p. 230—232° (Unger [5] gives m. p. 233°).

(b) *Sulphide* (III). The alkaline solution was steam-distilled, the distillate extracted with ether (3 × 80 c.c.), and the ether washed, dried (Na_2SO_4), and evaporated. The residual oil, b. p. 238—241°, was identified as 2-methylbenzothiazole (50%) by preparation of its picrate, m. p. 156°.[6]

(c) *Sulphide* (IV). The ether extract [obtained as in (b)] was washed with dilute hydrochloric acid, then water, and dried. Evaporation of the ether left acetophenone (68%)

[6] Finar and Montgomery, *J.*, 1960, 483; contrast Clark, *J.*, 1928, 2319.

(identified as its semicarbazone). The acid extract was neutralised with 10% aqueous sodium hydroxide, and extracted with ether, etc. [as in (b)], to give 2-methylbenzothiazole (40%).

(d) *Sulphide* (V). The ether extract [obtained as in (b)] was washed successively with dilute sodium hydroxide, water, dilute hydrochloric acid, and water, and dried. Distillation of the ether left acetophenone (40%). The alkaline extract was acidified with hydrochloric acid, the solution extracted with ether, and the ether extract washed, dried, and evaporated to give, on recrystallisation from water, benzoic acid (40%), m. p. 120—121°. The acid extract was neutralised with dilute sodium hydroxide, and extracted with ether, which was dried and distilled off to leave 2-methylbenzothiazole (35%).

Fission of Dibenzoylmethane.—Dibenzoylmethane (5 g.) in the stannous chloride solution (50 c.c.) was refluxed for 4—6 hr. The cooled solution was neutralised and steam-distilled. The distillate was extracted with ether (3 × 50 c.c.), and the ether extracted with dilute sodium hydroxide solution, then water, and dried. Evaporation of the ether left acetophenone (50%). The alkaline extract was acidified and extracted with ether (3 × 50 c.c.), and the ether dried and distilled to leave, on recrystallisation from water, benzoic acid (40%).

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66. 2-*Phenylbutadiene from* α-*Methylstyrene.*

By E. G. E. HAWKINS and R. D. THOMPSON.

The Prins reaction of α-methylstyrene, when carried out in acetic acid solution, has been found to give 3-phenylbut-2-enyl acetate, in addition to the 3-phenylbut-3-enyl acetate and 4-acetoxy-2-phenylbutan-2-ol previously reported. Pyrolysis of these phenylbutenyl acetates provides many by-products in addition to 2-phenylbutadiene, and a more satisfactory route to the diene involves catalytic dehydration of the isomeric phenylbutenols with iodine.

Conversion of the phenylbutenols into the corresponding chlorides and ethers has been studied. A second crystalline isomer of 2-phenylbutadiene dimer has been isolated.

IT has been reported by Price *et al.*[1] that treatment of α-methylstyrene with paraformaldehyde in boiling acetic acid for three hours, followed by removal of half of the acid and further heating after addition of acetic anhydride, gives a 70% yield of 3-phenylbut-3-enyl acetate, which could be converted into 2-phenylbutadiene on pyrolysis. Other workers, by pyrolysis of phenylbutenyl acetate prepared in this way, have claimed diene yields of 34%[2] and " nearly quantitative " (on recycle).[3]

Repetition of the reaction between α-methylstyrene and paraformaldehyde, under the conditions used by Price *et al.*, was found to yield a 3—4 : 1 mixture of 3-phenylbut-3- and -2-enyl acetate, in addition to some of the presumed precursor, 4-acetoxy-2-phenylbutan-2-ol, through its incomplete dehydration, and residues. Proof of the structure of the 3-phenylbut-2-enyl acetate, which was separated from its lower-boiling isomer by fractional distillation, was based on spectroscopic evidence together with the results of ozonolysis (to give acetophenone) and hydrogenation (to 3-phenylbutyl acetate). In view of the evidence of St. Pfau and Plattner[4] that dehydration of 1,3-diols (including 3-phenylbutane-1,3-diol) by acetic anhydride yields only βγ-unsaturated alcohols, the production of the ester of this αβ-unsaturated alcohol is unexpected: however, it was confirmed that dehydration of 4-acetoxy-2-phenylbutan-2-ol by acetic anhydride yielded a similar mixture of phenylbutenyl acetates.

[1] Price, Benton, and Schmidle, *J. Amer. Chem. Soc.*, 1949, **71**, 2860.
[2] Grummitt and Leaver, *J. Amer. Chem. Soc.*, 1952, **74**, 1595.
[3] Meek, Merrow, Ramey, and Cristol, *J. Amer. Chem. Soc.*, 1951, **73**, 5563.
[4] St. Pfau and Plattner, *Helv. Chim. Acta*, 1932, **15**, 1250.

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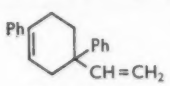
When α-methylstyrene and paraformaldehyde were heated for 1 hr. in acetic acid alone the product consisted of a mixture of the phenylbutenyl acetates and the glycol acetate, together with some of the free phenylbutenols.

Pyrolysis of the phenylbutenyl acetates, either separately or as a mixture, proved to be an unsatisfactory method of preparing 2-phenylbutadiene. These esters were dropped, either neat or in a diluent, down a heated glass or stainless steel tube, in a nitrogen atmosphere, and even when an inert column packing (glass beads) and optimum temperature (425—475°) and contact time were used, yields of diene never exceeded *ca.* 40%. The phenylbutadiene was always accompanied by α-methylstyrene and higher-boiling materials. Replacement of the inert column packing by active materials (*e.g.*, alumina or phosphoric acid on kieselguhr) led to a mixture of aromatic hydrocarbons, including ethylbenzene, cumene, naphthalene, and biphenyl.

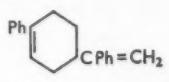
When mixed phenylbutenyl acetates, containing some of the free alcohols and glycol acetate, was recycled to the pyrolysis system (glass beads) a number of times and the final products were fractionated these contained, in addition to acetic acid, 2-phenylbutadiene, and unchanged material, also α-methylstyrene, 1-methylindene, acetophenone, 2-phenylbut-3-en-2-ol, and phenylbutadiene dimers, as well as a number of unidentified materials and polymeric residue. The 1-methylindene probably arose by cyclisation of a phenylbutenol or its ester, but in order to cast light on the sources of the other by-products of pyrolysis a number of related compounds were individually pyrolysed under similar, non-catalysed conditions.

Both 3-phenylbut-3- and -2-en-1-ol underwent a reverse Prins reaction, the latter more sluggishly, at 450—550°, to give mainly α-methylstyrene and formaldehyde, whilst 2-phenylbut-3-en-2-ol yielded a mixture including acetophenone and 1-methylindene and much polymeric material. The glycol acetate (4-acetoxy-2-phenylbutan-2-ol) also provided a mixture which contained some α-methylstyrene and acetic acid but whose largest constituent (40—45%) was 2-phenylbut-3-en-2-ol: its formation implied that loss of acetic acid from the primary acetate group was faster under these conditions than the dehydration of the tertiary alcohol. The free glycol, at 500°, also gave small quantities of α-methylstyrene but, surprisingly, was converted mainly into acetophenone: ethylene could not be detected in the exit gases, although either it or ethanol might have been expected.

Formation of 2-phenylbutadiene dimers under the conditions of pyrolysis is not unexpected: the monomer dimerises even at *ca.* 0°, and more rapidly at higher temperatures. Alder and Haydn,[5] who had previously noted the ease of dimerisation of this diene, isolated only one, (I), of the four possible isomers as a crystalline product. In the present work it was found that although compound (I), m. p. 61—62°, was the major constituent a second crystalline component (II), m. p. 56·5—58°, could be separated: its structure was confirmed by spectroscopic study and by dehydrogenation to 4-α-methylbenzylbiphenyl which was synthesised for comparison.



(I)



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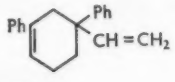

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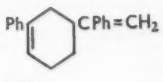

(IV)

Attempts were also made to obtain 2-phenylbutadiene by preparation and dehydrochlorination of the isomeric 4-chloro-2-phenylbutenes. Reaction of 3-phenylbut-3-en-1-ol with thionyl chloride in (i) dimethylaniline at 0°, (ii) benzene under reflux, and (iii) dimethylaniline and benzene at 0° gave some of the corresponding chloride, but the crude product was unstable on distillation and yielded varying amounts of 2-phenylbutadiene and its dimers on fractionation. Goering, Nevitt, and Silversmith's method,[6] namely,

[5] Alder and Haydn, *Annalen*, 1950, **570**, 201.
[6] Goering, Nevitt, and Silversmith, *J. Amer. Chem. Soc.*, 1955, **77**, 4042.

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reaction in ether at room temperature, gave 70—75% yields of the chloride. This reaction afforded also a small amount of 3-phenylthiophen, identified by synthesis. 3-Phenylbut-2-en-1-ol was similarly converted into its chloride, which appeared to be even more unstable than its isomer.

Dehydrochlorination of 4-chloro-2-phenylbut-1-ene by basic reagents proved difficult. It did not react with potassium hydroxide or sodium methoxide at room temperature, and only slightly under reflux. Use of sodium butoxide in boiling butan-1-ol led to decomposition, but little 2-phenylbutadiene was isolated: the main products were the diene dimer and butyl phenylbutenyl ether. Dimethylaniline at 300° and solid potassium hydroxide at 170° also had little effect, but yields of 50—60% of phenylbutadiene were obtained by use, at 140°, of sodium dissolved in diethylene glycol. By contrast, it has been reported [7] that 3-chloro-3-phenylbut-1-ene is dehydrochlorinated to 2-phenylbutadiene when heated with pyridine.

The most convenient route to 2-phenylbutadiene involved dehydration of the isomeric phenylbutenols or 3-phenylbutane-1,3-diol by heating them with catalytic amounts of iodine. Yields of the monomeric diene were usually 80—85%; it was free from α-methylstyrene, and the only other product appeared to be the diene dimer (as residue). 3-Phenylbut-2-en-1-ol is dehydrated, under these conditions, more rapidly than its isomer, whilst by suitable choice of column take-off temperature during the dehydration of the glycol a mixture of the intermediates, 3-phenylbut-3- (70%) and -2-en-1-ol (30%), was obtained in the distillate.

Treatment of 2-phenylbut-3-en-2-ol with dilute sulphuric acid provided mainly di-(3-phenylbut-2-enyl) ether; the intermediate alcohol, 3-phenylbut-2-en-1-ol, formed by anionotropic rearrangement of the tertiary alcohol, was also found in the product, and its acetate was obtained when the sulphuric acid was replaced by a mixture of acetic acid and anhydride. When ethanol was used as reaction solvent the major product was the ethyl ether of 3-phenylbut-2-en-1-ol. Examination by gas-phase chromatography showed that the latter alcohol with ethanol in the presence of hydrochloric acid gave 4-ethoxy-2-phenylbut-1-ene (*ca.* 12%) and *cis*- and *trans*-4-ethoxy-2-phenylbut-2-ene (88%). 3-Phenylbut-3-en-1-ol, when treated similarly, was partially converted into 3-phenylbut-2-en-1-ol and its ethyl ethers. Hydrogenation of the mixed ether isomers yielded solely ethyl 3-phenylbutyl ether, identical with a sample synthesised from 3-phenylbutyl chloride and sodium ethoxide.

In the absence of a reactive solvent acid-catalysed reaction of the phenylbutenols gave a high-boiling product. Although this gave no ether band in its infrared spectrum it was shown to be di-(3-phenylbut-2-enyl) ether (*a*) by synthesis from 3-phenylbut-2-enyl chloride and sodium 3-phenylbut-2-enyl oxide, and (*b*) by hydrogenation of it and the synthetic ether to the same di-(3-phenylbutyl) ether (having an ether band in the infrared spectrum) which was also obtained, in poor yield, by Williamson synthesis.

3-Phenylbut-3-en-1-ol with formic acid provided the formate in good yield, whereas 3-phenylbut-2-en-1-ol, under similar conditions, gave a poor yield of ester together with high-boiling ethers.

Experimental

Reaction of α-Methylstyrene, Paraformaldehyde, and Acetic Acid.—(*a*) (Cf. ref. 1.) Paraformaldehyde (110 g.), α-methylstyrene (354 g.), and acetic acid (1 l.) were heated together under reflux for 3 hr., part of the acetic acid (500 c.c.) was evaporated at normal pressure and replaced by acetic anhydride (500 c.c.), and heating was continued for a further 3 hr. The crude phenylbutenyl acetate (262 g.), b. p. 130—150°/15 mm., was separated by flash distillation. A number of similar batches were combined and fractionated in a 4 ft., helices-packed, heated column, to give main fractions: (i) (*ca.* 75%) b. p. 135°/13 mm., n_D^{20} 1·5233; (ii) (*ca.* 25%) b. p. 144—145°/13 mm., n_D^{20} 1·5335.

[7] Marvel and Woolford, *J. Org. Chem.*, 1958, **23**, 1658.

Fraction (i) was 3-phenylbut-3-enyl acetate (Found: C, 75·5; H, 7·4. Calc. for $C_{12}H_{14}O_2$: C, 75·8; H, 7·4%): the presence of vinyl and acetate groups was confirmed by the infrared spectrum, and ozonolysis yielded formaldehyde (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 163—166°). Hydrolysis with aqueous-alcoholic potassium hydroxide yielded 3-phenylbut-3-en-1-ol, b. p. 130—131°/13 mm., n_D^{20} 1·5581 (Found: C, 79·9; H, 8·2. Calc. for $C_{10}H_{12}O$: C, 81·1; H, 8·1%), which provided a 3,5-*dinitrobenzoate*, m. p. 77—78° (from ethanol) (Found: C, 59·3; H, 4·2; N, 7·8. $C_{17}H_{14}N_2O_6$ requires C, 59·7; H, 4·1; N, 8·2%), and a *phenylurethane*, m. p. 46—48° (Found: C, 76·1; H, 6·5; N, 5·1. $C_{17}H_{17}NO_2$ requires C, 76·4; H, 6·4; N, 5·2%). Hydrogenation of the alcohol (5 g.) in the presence of Adams catalyst gave 3-phenylbutanol (4·5 g.), b. p. 117—120·5°/12 mm., n_D^{20} 1·5190 (3,5-dinitrobenzoate, m. p. and mixed m. p. 73—74°).

Fraction (ii) consisted of 3-phenylbut-2-enyl acetate; its infrared and ultraviolet spectra were in agreement with this, and ozonolysis gave acetophenone (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 242—244°). Hydrolysis yielded 3-*phenylbut-2-en-1-ol*, b. p. 142—145°/15 mm., n_D^{20} 1·5698 (Found: C, 79·9; H, 8·2%), which afforded a 3,5-*dinitrobenzoate*, m. p. 143—145° (from acetone) (Found: C, 59·6; H, 4·14; N, 8·2%), and a *phenylurethane*, m. p. 80—82° (from ethanol–light petroleum) (Found: C, 76·2; H, 6·6; N, 5·1%). Catalytic hydrogenation gave, as before, 3-phenylbutanol, n_D^{20} 1·5181 (3,5-dinitrobenzoate as above).

(*b*) α-Methylstyrene (118 g.), paraformaldehyde (36 g.), and acetic acid (333 c.c.) were heated under reflux for 1 hr., the acid removed under reduced pressure, and the residue fractionated. There were obtained (i) α-methylstyrene (6·0 g.), (ii) fractions (48·4 g.) consisting of a mixture of 3-phenylbut-3- and -2-enyl acetate together with some of the corresponding alcohols and 4-methyl-4-phenyl-1,3-dioxan (7%), (iii) 4-acetoxy-2-phenylbutan-2-ol (68·4 g.), b. p. 160—165°/13 mm., n_D^{20} 1·5147 (Found: C, 69·3; H, 7·8. Calc. for $C_{12}H_{16}O_3$: C, 69·2; H, 7·7%), and (iv) high-boiling materials (7·7 g.).

Hydrolysis of 4-acetoxy-2-phenylbutan-2-ol (100 g.) yielded the corresponding glycol (60·5 g.), b. p. 167°/12 mm., n_D^{20} 1·5393 (Found: C, 72·9, 72·8; H, 8·5, 8·6. Calc. for $C_{10}H_{14}O_2$: C, 72·3; H, 8·4%), which provided a *monophenylurethane*, m. p. 110—112° (from benzene–light petroleum) (Found: C, 72·0; H, 6·7; N, 5·0. $C_{17}H_{19}NO_3$ requires C, 71·6; H, 6·7; N, 4·9%). An attempt to prepare the 3,5-dinitrobenzoate of this glycol brought about dehydration and there was isolated the slightly impure derivative of 3-phenylbut-2-en-1-ol, m. p. 136—138°, undepressed on admixture with an authentic sample (Found: C, 60·0; H, 4·3; N, 8·0%).

Pyrolysis of Phenylbutenyl Acetates.—(*a*) The acetate (usually 25 g.) (3-phenylbut-3- or -2-enyl or the mixed ester) was allowed to drop slowly, in a stream of nitrogen, into a 2 ft. tube (of glass or stainless steel), which was heated in a furnace: the tube temperature was recorded by means of a thermocouple. The tube was packed to various depths, with glass beads, porcelain saddles, or activated alumina, and experiments were made with different temperatures and feed rates. The products, condensed in a carbon dioxide-cooled receiver, were distilled and examined spectroscopically. Selected results are given in Table 1.

TABLE 1.

Isomer used *	Wt. (g.)	Diluent	Length packed † (in.)	Temp.	Time (min.)	Product (g.) Phenylbutadiene ‡	Product (g.) High-boiling material
3	25	—	24	400°	85	0·9	18·3
3	25	—	7½	450	70	5·5	13·4
3	25	—	24	475	20	7·2	10·2
3	25	—	1½	500	65	7·2	13·6
2	25	—	1½	500	110	7·7	8·0
3	25	—	1½	550—575	25	5·1	12·4
3	25	Benzene (20 g.)	7½	400	105	0·5	23·6
3	25	,,	7½	450	120	5·5	11·9
2	25	,,	7½	450	65	7·7	9·8
3	25	Benzene	7½	450	150	6·0	13·1

* 3 = 3-Phenylbut-3-enyl acetate; 2 = 3-Phenylbut-2-enyl acetate. † Beads.
‡ Contains α-methylstyrene in varying amounts.

Addition of various metal salts or antioxidants to the feed did not appreciably reduce the proportion of high-boiling products. When the tube contained activated alumina as packing

the product at 300—450° was cumene (in low yield), containing ethylbenzene and α-methylstyrene; at 550—600° naphthalene and biphenyl were formed.

(*b*) Mixed isomers of phenylbutenyl acetate were pyrolysed in batches of 400 g. in a tube at 450° containing 7½ in. of glass beads (reaction time *ca.* 4½ hr.). The product was flash-distilled: the portion boiling at <100°/15 mm. was fractionated to separate it into acetic acid, α-methylstyrene, and 2-phenylbutadiene, and the material (A) with b. p. between that of the diene and 100°/15 mm. was set aside. The material with b. p. 100—200°/15 mm. was recycled for pyrolysis, after being made up with fresh ester; after three recycles it was set aside (B). All the residual material (b. p. >200°/15 mm.), containing polymers, was discarded. The material was refractionated, with results as in Table 2. Many of these fractions were complex mixtures, (A + B)

TABLE 2.

Fr.	B. p./13 mm.	Wt. (g.)	n_D^{20}	Fr.	B. p./13 mm.	Wt. (g.)	n_D^{20}
1	64—71°	13·5	1·5445	7	100—112°	9·7	1·5579
2	71—75	5·0	1·5445	8	112—118	11·7	1·5565
3	75—80	7·2	1·5480	9	118—122	17·9	1·5470
4	80—87	26·7	1·5558	10	122—124	20·5	1·5425
5	87—95	7·5	1·5529	11	124—132	14·2	1·5385
6	95—100	32·4	1·5459	12	132—140	13·7	1·5380
			−1·5465	13	140—155	4·0	1·5480

not resolved by gas-phase chromatography, but the main constituents were evaluated by this means and by their infrared spectra. Fraction 1 consisted largely of 2-phenylbutadiene, fractions 9—11 of 4-methyl-4-phenyldioxan (present in the feed), and fractions 11—13 of unchanged phenylbutenyl acetates.

Fraction 4 was redistilled to give 1-methylindene, b. p. 199—200°, n_D^{20} 1·5535, identical spectroscopically (infrared) with material, b. p. 81—85°/11 mm., synthesised by reaction of indan-1-one with methylmagnesium iodide. The product of this Grignard reaction was separated by fractionation into 1-methylindene, 1-methylindanol, and unchanged indan-1-one. Catalytic hydrogenation (Adams catalyst) of a portion of fraction 4 yielded 1-methylindane, b. p. 68—72°/13 mm., n_D^{20} 1·5200, identified by its infrared spectrum.

Fraction 6 was refractionated, to give 2-phenylbut-3-en-2-ol, b. p. 212—215°, n_D^{20} 1·5445, identical spectroscopically (infrared) with that obtained by pyrolysis of 4-acetoxy-2-phenylbutan-2-ol (see below).

Redistillation of the stored 2-phenylbutadiene, obtained from this series of pyrolyses, left a residue of dimer which had b. p. 210—220°/14 mm. Fractional crystallisation from ethanol and methanol yielded three batches (A), (B), and (C) of solid. (A) had m. p. 61—62° (Found: C, 92·3, 92·2; H, 7·65, 7·7. Calc. for $C_{20}H_{20}$: C, 92·3; H, 7·7%), and its ultraviolet and infrared spectra were in agreement with the structure of the dimer isolated by Alder and Haydn,[5] 1,4-diphenyl-4-vinylcyclohex-1-ene. When heated for 10 hr. at 320° with 5% palladium–charcoal it gave *p*-terphenyl, m. p. 210—212° (from chloroform) (Found: C, 94·2; H, 6·1. Calc. for $C_{18}H_{14}$: C, 93·9; H, 6·1%), identified spectroscopically.

Solid (B) had m. p. 56·5—58° (Found: C, 91·9; H, 7·6%). Its infrared spectrum disclosed an αα-disubstituted vinyl group, and ultraviolet spectroscopy indicated a vinylbenzene system. It was shown to be α-(4-phenylcyclohex-3-enyl)styrene (II) by dehydrogenation, as above, to 4-α-*methylbenzylbiphenyl*, m. p. 61·5—63° (from methanol) (Found: C, 93·0; H, 7·0. $C_{20}H_{18}$ requires C, 93·0; H, 7·0%), which was synthesised, for comparison, by the following steps: (i) Friedel–Crafts reaction between benzoyl chloride and biphenyl [8] gave 4-benzoylbiphenyl, m. p. 100—101°; (ii) reaction of this with methylmagnesium iodide [9] provided 4-biphenylyl-α-methylbenzyl alcohol, m. p. 102—104°; (iii) dehydration with sulphuric acid in acetic acid [9] gave α-4-biphenylylstyrene, m. p. 95—96°; and (iv) catalytic hydrogenation of this olefin (Adams catalyst) gave 4-α-methylbenzylbiphenyl, m. p. and mixed m. p. 62—63° (identical spectra).

Compound (C) had m. p. 40—44°, and was shown spectroscopically to be a 7 : 3 mixture of (A) and (B) although attempts at separation by crystallisation failed.

In addition to materials (A—C) a non-crystalline portion remained, but dehydrogenation gave a product in which only *p*-terphenyl could be identified.

[8] Schlenk and Bergmann, *Annalen*, 1928, **463**, 120.
[9] Schlenk and Bergmann, *Annalen*, 1928, **464**, 22.

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Pyrolysis of 3-*Phenylbut*-3-*en*-1-*ol*.—The alcohol (25 g.) was dropped through a 2 ft. tube, containing 7½ in. of glass beads and heated to 450°, during 1 hr., and the condensed product distilled. The distillate (16·1 g.), b. p. 53°/12 mm., n_D^{20} 1·5380, was shown spectroscopically to be α-methylstyrene. During the pyrolysis and distillation paraformaldehyde crystallised on the colder surfaces.

Pyrolysis of 3-*Phenylbut*-2-*en*-1-*ol*.—Use of the above conditions led to little reaction, but when the column temperature was raised to 550° the phenylbutenol (15 g.) yielded paraformaldehyde and fractions: (i) (3·2 g.) b. p. <55—60°/12 mm., n_D^{20} 1·5346; (ii) (1·0 g.) b. p. 60—80/12 mm., n_D^{20} 1·5502; (iii) (1·4 g.) b. p. 80—122°/12 mm., n_D^{20} 1·5620; (iv) (3·3 g.) b. p. 122—137°/12 mm., n_D^{20} 1·5633; and residue (1·1 g.). Spectroscopy showed that fractions (i) and (ii) contained α-methylstyrene, biphenyl, 1-methylindene, and other aromatic hydrocarbons, whilst fraction (iv) was unchanged phenylbutenol.

Pyrolysis of 2-*Phenylbut*-3-*en*-2-*ol*.—The alcohol (15 g.), pyrolysed over glass beads at 550°, yielded fractions shown spectroscopically to contain acetophenone and 1-methylindene; much dark red residue (7·2 g.), remained.

Pyrolysis of 4-*Acetoxy*-2-*phenylbutan*-2-*ol*.—The glycol monoacetate (300 g.) was pyrolysed in the system described above, at 500°, during 9⅓ hr. Distillation of the product yielded acetic acid (32 g.), α-methylstyrene (33·5 g.), a fraction (87·0 g.), b. p. 97—98°/12 mm., n_D^{20} 1·5331—1·5341, and a residue (23·2 g.). Redistillation of part of the above fraction yielded 2-phenylbut-3-en-2-ol, b. p. 148—149°/100 mm., n_D^{20} 1·5330 (Found: C, 80·7; H, 8·1. Calc. for $C_{10}H_{12}O$: C, 81·1; H, 8·1%), which gave a *phenylurethane* (in low yield on long heating with phenyl isocyanate), m. p. 107—108·5° (Found: C, 76·4; H, 6·4; N, 5·1. $C_{17}H_{17}NO_2$ requires C, 76·4; H, 6·4; N, 5·2%), and the 3,5-dinitrobenzoate, m. p. and mixed m. p. 141—143°, of 3-phenylbut-2-en-1-ol. Catalytic hydrogenation (Adams catalyst) provided 2-phenylbutan-2-ol, b. p. 94—96°/13 mm., n_D^{20} 1·5200, identified spectroscopically.[10]

For comparison, 2-phenylbut-3-en-2-ol was synthesised from vinylmagnesium chloride and acetophenone in tetrahydrofuran.[7] Distillation of the product gave fractions containing mixtures of acetophenone and the alcohol in varying proportions: the purest sample, b. p. 97°/12 mm., n_D^{20} 1·5336, contained 95% of the phenylbutenol and 5% of acetophenone.

Pyrolysis of 3-*Phenylbutane*-1,3-*diol*.—The glycol (11 g.) was dropped at 500° during 115 min., through the above column. Distillation of the product gave: (i) (1·4 g.) b. p. 50—75°/12 mm., n_D^{20} 1·5364; (ii) (3·0 g.), b. p. 75—90°/12 mm., n_D^{20} 1·5345; (iii) (2·5 g.) b. p. 90—160°/12 mm., n_D^{20} 1·5354; and residue (0·5 g.). Infrared spectroscopy showed that fraction (i) contained α-methylstyrene (65%) and acetophenone (35%) (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 249°), fraction (ii) was mainly acetophenone (95%), and fraction (iii) was the glycol.

Pyrolysis of Dimers of 2-*Phenylbutadiene*.—(i) 1,4-Diphenyl-4-vinylcyclohex-1-ene (16 g.), pyrolysed at 550—560° during 65 min., gave a product which by fractionation and infrared spectroscopy was shown to contain 2-phenylbutadiene, 1-methylindene, biphenyl, and *p*-terphenyl.

(ii) Crude mixed isomers, treated similarly, gave a similar product, but in addition to *p*-terphenyl, m. p. 210—212° (Found: C, 94·2; H, 6·1. Calc. for $C_{18}H_{14}$: C, 93·9; H, 6·1%), there was also isolated *m*-terphenyl, m. p. 83—84° (from methanol) (Found: C, 94·1; H, 6·0%), identified spectroscopically.

Conversion of Phenylbutenols into their Chlorides.—(a) 3-*Phenylbut*-3-*en*-1-*ol*. (i) The alcohol (50 g.) was added, during 1 hr., to thionyl chloride (42 g.) in ether (150 c.c.) at room temperature, and stirring continued for a further ½ hr. The solvent was evaporated and the product flash-distilled: the distillate (48·2 g.) had b. p. 100—120°/11 mm. Redistillation gave 4-*chloro*-2-*phenylbut*-1-*ene* (42·1 g.), b. p. 106—107°/11 mm., n_D^{20} 1·5504 (Found: C, 72·65; H, 6·7. $C_{10}H_{11}Cl$ requires C, 72·1; H, 6·6%).

(ii) Repetition of experiment (i) on half the scale, up to the end of the reaction with thionyl chloride, was followed by washing of the ethereal solution with water and sodium hydrogen carbonate solution, and storage for 2 days over anhydrous sodium sulphate and solid sodium hydrogen carbonate. Distillation then gave 2-phenylbutadiene (8·5 g.), n_D^{20} 1·5469, and its dimers (5·7 g.), but no chloride.

(iii) Repetition of experiment (i) on double the scale yielded, on final distillation, 2-phenylbutadiene (20 g.), 4-chloro-2-phenylbut-1-ene (52 g.), and a fraction (6 g.), b. p. 110—120°/11 mm., which crystallised on storage. Recrystallisation from light petroleum (b. p.

[10] Hawkins, *J.*, 1949, 2076.

60—80°) and methanol gave 3-phenylthiophen, m. p. 88—90° (Found: C, 75·0; H, 5·2; S, 19·4. Calc. for $C_{10}H_8S$: C, 75·0; H, 5·0; S, 20·0%). 3-Phenylthiophen was synthesised for comparison by heating 2-phenylbutadiene (22 g.) and sulphur (16 g.) at 200° for 6½ hr.: in addition to polymer (26 g.), there was obtained a distillate (5·9 g.) which after several recrystallisations from ethanol had m. p. and mixed m. p. 92—94° (lit.,[11] 91·5—92°) (Found: C, 75·1; H, 5·0; S, 19·9%).

Decomposition with formation of 2-phenylbutadiene and its dimers occurred on reaction of the phenylbutenol with thionyl chloride in *NN*-dimethylaniline at 0°, in benzene under reflux, or in *NN*-dimethylaniline and benzene at 0°.

(b) *3-Phenylbut-2-en-1-ol.* The alcohol (75 g.) was added to thionyl chloride (63 g.) in ether (225 c.c.) as above. Flash-distillation of the product gave a distillate (79·5 g.), b. p. 100—118°/11 mm., which on fractionation yielded 1-chloro-3-phenylbut-2-ene (25·7 g.), b. p. 97—110°, n_D^{20} 1·5580. Other products, including 2-phenylbutadiene and its dimer, were also obtained.

Dehydrochlorination of 4-Chloro-2-phenylbut-1-ene.—The chloride (8·3 g.) was added to a solution from sodium (1·25 g.) in diethylene glycol (20 c.c.) and the mixture heated, at 100—140°, under a packed column at reduced pressure: the low-boiling product (b. p. 55—60°/11 mm.) was removed as rapidly as possible. Redistillation yielded 2-phenylbutadiene (3·8 g.), b. p. 57—59°/11 mm., n_D^{20} 1·5480.

Other attempts at dehydrochlorination gave either no or little reaction: these included the use of potassium hydroxide, in methanol at 35° and fused (at 160°), sodium methoxide solution under reflux, and dimethylaniline at 150°. Sodium n-butoxide solution at 180° gave a mixture including a fraction shown spectroscopically to contain an ether group.

Dehydration of Phenylbutenols, etc., with Iodine.—(a) *3-Phenylbut-3-en-1-ol.* The alcohol (10 g.) was heated at *ca.* 140—150° with a crystal of iodine under a heated, helices-packed column at reduced pressure. Wet phenylbutadiene was taken off as formed: after drying there was obtained pure 2-phenylbutadiene (6·9 g.), b. p. 59—60°/12 mm., n_D^{20} 1·5461, with residue (2·0 g.).

(b) *3-Phenylbut-2-en-1-ol.* The alcohol was treated as above, to give finally 2-phenylbutadiene (7·2 g.) and residue (1·9 g.).

(c) *3-Phenylbutane-1,3-diol.* (i) The glycol (10 g.) was dehydrated as above, except that material with b. p. <140°/10 mm., was removed rapidly through a column. The distillate (6·6 g.), b. p. 120—140°/10 mm., n_D^{20} 1·5530, was found, by infrared spectroscopy, to contain 3-phenylbut-3- (70%) and 3-phenylbut-2-en-1-ol (30%); there was a residue (1·4 g.).

(ii) Repetition of the above experiment, but under the conditions of (a) and (b) with a low temperature of take-off, led to the conversion of the glycol (10 g.) into 2-phenylbutadiene (6·5 g.) and residue (1·9 g.).

(d) *4-Acetoxy-2-phenylbutan-2-ol.* Dehydration of the glycol acetate (10 g.) under similar conditions to (c, i) gave a distillate (7·7 g.), b. p. 115—140°/10 mm., n_D^{20} 1·5297, shown spectroscopically to consist of 4-acetoxy-2-phenylbut-1-ene (70%), 4-acetoxy-2-phenylbut-2-ene (20%), and glycol acetate (10%).

Ethyl Phenylbutenyl Ethers.—(a) *From 3-phenylbut-2-en-1-ol.* (i) The alcohol (40 g.) and ethanol (100 c.c.), containing a few drops of hydrochloric acid, were heated together under reflux for 3 hr. After working up there was obtained an ethyl phenylbutenyl ether (29·9 g.), b. p. 118°/11 mm., n_D^{20} 1·5268; its infrared spectrum showed an absence of hydroxyl and the presence of an ether group, mainly with unsaturation of the type CRR′:CHR″ but having *ca.* 5% of type CH_2:CRR′.

(ii) Reaction as in experiment (i) but on half the scale and with heating continued for 16 hr. gave fractions (i) (1·4 g.) b. p. 60—110°/11 mm., n_D^{20} 1·5385, (ii) (3·0 g.) b. p. 110—116°/11 mm., n_D^{20} 1·5189, (iii) (6·2 g.) b. p. 116—120°/11 mm., n_D^{20} 1·5235; (iv) (1·6 g.) b. p. 120—125°/11 mm., n_D^{20} 1·5224, and (v) (0·2 g.) b. p. 215—220°/11 mm., and a residue (2·8 g.). Examination of fractions 2—4 spectroscopically and fractions 2 and 3 by gas chromatography showed that they contained three isomeric ethyl ethers, *i.e.*, *cis-* and *trans*-1-ethoxy-3-phenylbut-2-ene and 4-ethoxy-2-phenylbut-1-ene: the first two (the major constituents) had similar infrared spectra; the third occurred to the extent of *ca.* 12%.

(b) *From 3-phenylbut-3-en-1-ol.* The phenylbutenol (10 g.) was heated with acidified ethanol for 18 hr.; spectroscopy showed the main fractions obtained [(1·5 g.) b. p. 113—

[11] Broun and Voronkov, *J. Gen. Chem.* (*U.S.S.R.*), 1947, **17**, 1162.

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117°/11 mm., n_D^{20} 1·5268; (4·1 g.) b. p. 117—120°/11 mm., n_D^{20} 1·5338] to be mixtures of unchanged phenylbutenol (25%) with 1-ethoxy-3-phenylbut-2-ene.

(c) *From 2-phenylbut-3-en-2-ol.* Similar treatment again yielded 1-ethoxy-3-phenylbut-2-ene, b. p. 120—124°/12 mm., n_D^{20} 1·5273.

The mixed isomers from experiment (a, ii) were hydrogenated over Adams catalyst to yield *1-ethoxy-3-phenylbutane*, b. p. 100—100·5°/11 mm., n_D^{20} 1·4879, uniform on gas chromatography (Found: C, 80·2; H, 10·1. $C_{12}H_{18}O$ requires C, 80·9; H, 10·1%), and identical spectroscopically with a synthetic sample. The latter was obtained by heating 3-phenylbutyl chloride (7·2 g.) with sodium ethoxide (from 3 g. of sodium in 50 c.c. of ethanol) and toluene (50 c.c.) for 58 hr. The 1-ethoxy-3-phenylbutane (3·1 g.) finally obtained had b. p. 100—101·5°/11 mm., n_D^{20} 1·4875 (Found: C, 81·15; H, 10·0%), and was uniform on gas chromatography.

Di(phenylbutenyl) Ether.—(a) *From 2-phenylbut-3-en-2-ol.* The alcohol (5 g.) and 1% hydrochloric acid (40 c.c.) were heated together on the water-bath for 1½ hr. and the cooled product was extracted with ether. Final distillation yielded unchanged phenylbutenol and a fraction (2·3 g.), b. p. 215—220°/12 mm., n_D^{20} 1·5842 (Found: C, 85·3; H, 7·9. $C_{20}H_{22}O$ requires C, 86·3; H, 7·9%), having only weak ether bands (infrared spectrum) but with a double bond conjugated with an aromatic ring (ultraviolet spectrum). The infrared spectrum also indicated that unsaturation was not of the CRR′:CH_2 type, in agreement with the product's being di-(3-phenylbut-2-enyl) ether. Catalytic hydrogenation (Adams catalyst) yielded di-(3-phenylbutyl) ether, identical with that synthesised as below.

(b) *From 3-phenylbut-2-en-1-ol.* The alcohol (10 g.), 1% hydrochloric acid (20 c.c.), and dioxan (5 c.c.) were heated on the steam-bath for 4 hr. Working up gave di-(3-phenylbut-2-enyl) ether (4·5 g.), identically spectroscopically with that above, and a residue (3·0 g.).

(c) *From 3-phenylbutane-1,3-diol.* The glycol (10 g.) and 20% sulphuric acid (25 c.c.) were heated under reflux for 3½ hr. Final distillation yielded the di(phenylbutenyl) ether (2·2 g.), b. p. 220—240°/12 mm., n_D^{20} 1·5920, and higher-boiling materials (4·2 g.).

(d) *Synthetic.* Sodium (0·6 g.) was dissolved in 3-phenylbut-2-en-1-ol (20 c.c.) and toluene (25 c.c.) under reflux, and 1-chloro-3-phenylbut-2-ene (4·0 g.) added gradually. Heating at 70° and stirring were continued for 2 hr., *ca.* 80% of the sodium alkoxide being utilised. Distillation of the product gave a major fraction (8·3 g.), b. p. 200—230°/11 mm., which on redistillation provided fractions: (i) (2·7 g.) b. p. 203—215°/11 mm., n_D^{20} 1·5903; and (ii) (2·9 g.) b. p. 215—225°/11 mm., n_D^{20} 1·5845. The infrared spectra showed that fraction (i) was largely the di(phenylbutenyl) ether, but contained some dimer of 2-phenylbutadiene, whereas (ii) was the pure ether, identical with that from (a), (b), and (c) above.

The synthetic di(phenylbutenyl) ether, after hydrogenation (Adams catalyst), yielded the *di(phenylbutyl)ether*, b. p. 215—225°/12 mm., n_D^{20} 1·5379 (Found: C, 85·0; H, 9·1. $C_{20}H_{26}O$ requires C, 85·1; H, 9·2%), $\nu_{max.}$ 1125 cm.$^{-1}$ (ether).

The saturated ether was also obtained in poor yield (0·5 g.) by heating 1-chloro-3-phenylbutane (5 g.) with a solution from sodium (0·3 g.) in 3-phenylbutanol (5 g.) and toluene (25 c.c.) under reflux for 24 hr.

Reaction of Phenylbutenols with Formic Acid.—(a) *3-Phenylbut-3-en-1-ol.* The alcohol (10 g.) and formic acid (4 g.) were heated together at 130° for ½ hr. and the product distilled to give fractions: (i) (8·6 g.) b. p. 118—122°/12 mm., n_D^{20} 1·5367; (ii) (1·0 g.) b. p. 130—150°/12 mm., n_D^{20} 1·5367; and a residue (0·2 g.). Fraction (i) was *3-phenylbut-3-enyl formate* (Found: C, 75·15; H, 7·0. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·8%), having an infrared spectrum consistent with the presence of a CH_2:CRR′ system and a formate group.

(b) *3-Phenylbut-2-en-1-ol.* The alcohol (10 g.) was treated in the same way as its isomer (above). There were obtained fractions: (i) (2·0 g.) b. p. 125—130°/12 mm., n_D^{20} 1·5458; (ii) (2·9 g.) b. p. 190—225°/12 mm., n_D^{20} 1·5340; and a residue (3·2 g.). Spectroscopically, fraction (i) was shown to consist of the phenylbutenyl formate, but (ii) was unidentified.

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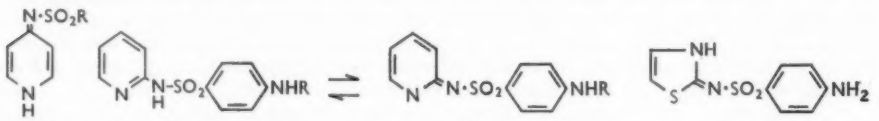
67. *Potentially Tautomeric Pyridines. Part III.*[1] 2-, 3-, *and* 4-*Methanesulphonamidopyridine.*

By R. Alan Jones and A. R. Katritzky.

The basicities and spectra of the compounds named in the title and alkylated derivatives of their alternative tautomeric forms show that the 2- and the 4-isomers exist largely in the imino-form and the 3-isomer predominantly in the sulphonamido-form.

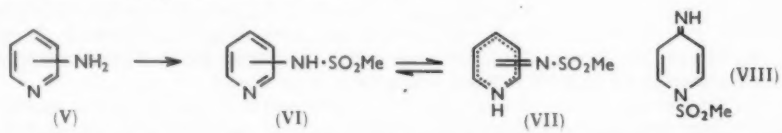
In Part II,[1] the tautomeric behaviour of acylaminopyridines was shown to resemble that of the corresponding aminopyridines and not the hydroxy-analogues. It was suggested that this was because the carbonyl group in pyrid-2- and -4-one acylimines is unable to conjugate simultaneously with the spare pair of electrons on the exocyclic nitrogen and with the aromatic system. Mesomerism involving sulphonyl groups is comparatively weak and thus for pyridone sulphonylimines (as I) destabilisation due to this factor should be unimportant, and therefore the tautomeric equilibrium should be displaced more in favour of the imine form. Shepherd, Bratton, and Blanchard [2] (who summarise earlier inconclusive work) showed by ultraviolet spectral comparison with the alkylated tautomers that acetylsulphapyridine existed in aqueous solution as 40% of form (II; R = Ac) and



(I) (II) (III) (IV)

60% of form (III; R = Ac), and that sulphathiazole existed predominantly as form (IV). Angyal and Warburton [3] reported similar findings for sulphathiazole and concluded that 30% of sulphapyridine existed as form (III; R = H) in aqueous solution (see also ref. 4). The above work was complicated by the occurrence in the sulpha-drugs of a second chromophore and basic centre.[5] We have now prepared 2-, 3-, and 4-methanesulphonamidopyridine and methylated derivatives of their alternative tautomeric forms and studied their spectra and basicities.

Recently Russian workers [6] have investigated infrared and ultraviolet spectra of 2-methanesulphonamidopyridine and 2- and 4-benzenesulphonamidopyridine and methylated derivatives of the fixed tautomeric forms. They conclude that the compounds exist in the imino-form in the solid state and predominantly so in aqueous solution. The present work confirms and amplifies these results.



(V) (VI) (VII) (VIII)

Preparation of Compounds.—2-, 3-, and 4-Aminopyridine reacted with methanesulphonyl chloride to give the corresponding methanesulphonamido-derivatives (V ⟶ VI, VII). These products were not the isomeric compounds methanesulphonylated at the ring nitrogen (cf. VIII) because each product could be converted into two methyl

[1] Part II, Jones and Katritzky, *J.*, 1959, 1317.
[2] Shepherd, Bratton, and Blanchard, *J. Amer. Chem. Soc.*, 1942, **64**, 2532.
[3] Angyal and Warburton, *Austral. J. Sci. Res.*, 1951, **44**, 93.
[4] Sheinker and Kuznetsova, *Zhur. fiz. Khim.*, 1957, **31**, 2656.
[5] Cf. Vandenbelt and Doub, *J. Amer. Chem. Soc.*, 1944, **66**, 1633.
[6] Sheinker, Peresleni, Zosimova, and Pomerantsev, *Russ. J. Phys. Chem.*, 1959, **33**, 303.

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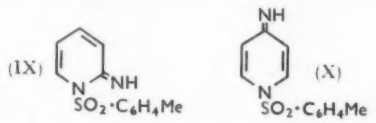
derivatives, in which the sulphonyl group was attached to the exocyclic nitrogen atoms (see below), and the ultraviolet spectra of the cationic species resemble those of one of the methylated derivatives (of known structure, see below) in the same series.

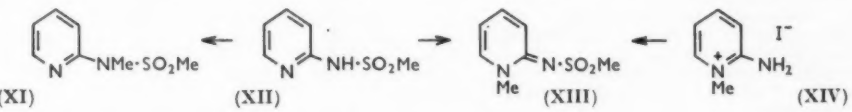
Angyal and his co-workers [7] also provided evidence that, while sulphonylation of amino-heteroaromatic compounds occurs initially on the ring-nitrogen atom, the products rearrange spontaneously to the isomers with the sulphonyl group attached to the exocyclic nitrogen atom.

Grammaticakis [8] assigned the structures (IX) and (X) to sulphonamides from 2- and 4-aminopyridine because their ultraviolet spectra differ from those of acylaminopyridines.



It appeared more likely that these products have the (tautomeric) toluenesulphonamidopyridine structure, and the similarity of their ultraviolet spectra to those of the analogous methanesulphonamido-compounds (Fig. 1) supports this view.

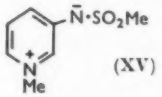
2-Methanesulphonamidopyridine and diazomethane gave two products; that obtained in lower yield was identical with the product obtained by use of dimethyl sulphate and



alkali and was shown to be (XIII) by its formation from 2-amino-1-methylpyridinium iodide (XIV). Further, 2-(*N*-methylmethanesulphonamido)pyridine (XI) gave the bands characteristic of the 2-substituted pyridine ring [9] at 1594 (220), 1576 (65), 1472 (210), 1441 (160), 1277 (70), (—), (—), 991 cm.$^{-1}$ (35); † the other bands were characteristic of the NMe·SO_2Me substituent.[10]

4-Methanesulphonamidopyridine also gave two products with diazomethane; structures were assigned on the basis of the infrared spectra. 4-(*N*-Methylmethanesulphonamido)-pyridine showed bands characteristic of the 4-substituted pyridine ring [11] at 1595 (300), 1564 (50), 1497 (120), 1432 (20), (—), 996 (75), 815 (85) and those of the NMe·SO_2Me substituent.[10]

Only one product was isolated from the reaction of 3-methanesulphonamidopyridine with diazomethane; its infrared spectrum showed bands at 1587 * (25), 1577 (30), 1483 (140), 1426 (125), (—), 1127 * (35), 1106 (15), (—), 1023 (75), 805 * (35) characteristic of the 3-substituted pyridine nucleus.[12] The isomeric zwitterion (XV) was obtained as the perchlorate *via* the action of methotoluene-*p*-sulphonate.



(XV)

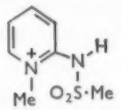
Basicity Measurements (Table 1).—4-Methanesulphonamidopyridine is a considerably weaker base than 4-(*N*-methylmethanesulphonamido)pyridine, but is comparable in strength to 1-methylpyrid-4-one methanesulphonylimine. Quantitatively the results indicate that the imino-form predominates by a factor of *ca.* 40 in the tautomeric equilibrium.

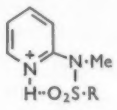
† For the significance of asterisks see Table 3; figures in parentheses denote ϵ_A values.

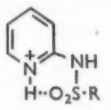
[7] Angyal, Morris, and Warburton, *Austral. J. Sci. Res.*, 1952, **5**, *A*, 367, 374.
[8] Grammaticakis, *Bull. Soc. chim. France*, 1959, 480.
[9] Katritzky and Hands, *J.*, 1958, 2202.
[10] Katritzky and Jones, *J.*, 1960, 4497.
[11] Katritzky and Gardner, *J.*, 1958, 2198.
[12] Katritzky, Hands, and Jones, *J.*, 1958, 3165.

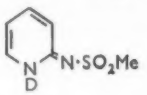
3-Methanesulphonamidopyridine is weaker as a base than anhydro-3-methanesulphonamido-1-methylpyridinium hydroxide by 1·12 pK units, and weaker than 3-(*N*-methylmethanesulphonamido)pyridine by 0·53 pK unit. This indicates that for the potentially tautomeric compound, the non-zwitterionic form (as VI) predominates over the zwitterionic by a factor of *ca.* 4—13.

For the 2-series, the situation is complicated by different amounts of hydrogen-bonding and steric hindrance in the various cations (XVI—XVIII). The relatively high basicity


(XVI)


(XVII)


(XVIII)


(XIX)

of 2-(*N*-methylmethanesulphonamido)pyridine reflects the need to lose a hydrogen-bonded proton from the cation. The somewhat lower basicity of 2-methanesulphonamidopyridine could be explained if the compound existed predominantly in the imino-form, and

TABLE 1. pK_a *of sulphonamidopyridines.*

Pyridine derivative	pK_a [a]	Stand. devn.	Concn. (10^{-4}M)	Wavelength (mμ)
2-Methanesulphonamido-	1·10	0·11	0·43	310
2-(*N*-Methylmethanesulphonamido)-	1·73	0·07	0·60	289
1-Methylpyrid-2-one methanesulphonylimine	−0·33	0·04	0·31	312
3-Methanesulphonamido-	3·43	0·03	449·0	—
2-(*N*-Methylmethanesulphonamido)-	3·94	0·02	433·8	—
Anhydro-3-methanesulphonamido-1-methylpyridinium hydroxide	4·55	0·01	164·1	—
4-Methanesulphonamido-	3·64	0·06	222·2	—
4-(*N*-Methylmethanesulphonamido)-	5·14	0·04	111·6	—
1-Methylpyrid-4-one methanesulphonylimine	3·42	0·12	90·0	—
2-Methanesulphonamido-	8·02	0·01	145·5	—
3-Methanesulphonamido-	7·02	0·06	170·6	—
4-Methanesulphonamido-	9·07	0·08	222·2	—

[a] Arithmetical mean of six values. The first nine entries refer to proton addition, the last three to proton loss. [b] An entry in this column signifies that the determination was spectrometric; otherwise it was potentiometric.

TABLE 2. *Ultraviolet spectra (wavelengths in* mμ).

		Ions						Neutral species [b]			
	Pyridine derivative	λ	$10^{-3}\varepsilon$	λ	$10^{-3}\varepsilon$	λ	$10^{-3}\varepsilon$	λ	$10^{-3}\varepsilon$	λ	$10^{-3}\varepsilon$
1	2-Methanesulphonamido-	221	10·5	286	11·5			241	11·6	310	7·2
2		239	13·7	291	5·0						
3	2-(*N*-Methylmethanesulphonamido)-	227	6·4	289	7·7			220	5·9	265	3·5
4	1-Methylpyrid-2-one methanesulphonylimine	221	13·2	283	14·8			243	10·9	311	6·6
5	3-Methanesulphonamido-	205	17·4	234	6·3	284	4·2	263	3·2	320	0·3
6		244	11·5	292	3·0						
7	3-(*N*-Methylmethanesulphonamido)-	214	8·8	240	4·3	280	3·3	266	2·7		
8	Anhydro-3-methanesulphonamido-1-methylpyridinium hydroxide	208	22·2	236	6·0	287	3·9	262	14·1	325	3·6
9	4-Methanesulphonamido-			253	18·3			281	25·2		
10				253	17·2						
11	4-(*N*-Methylmethanesulphonamido)-			263	18·1			236	7·9		
12	1-Methylpyrid-4-one methanesulphonylimine			257·5	18·5			287	27·3		

[a] Nos. 2, 6, and 10 are anions measured in N-NaOH; the remainder are cations. Nos. 1, 3, and 4 were measured in 20N-H_2SO_4; Nos. 5, 7, and 8 in N-H_2SO_4; and Nos. 9, 11, and 12 in 10N-H_2SO_4. [b] All measured in a phosphate buffer of pH 10, except 1 (pH 4·6), 5 (pH 5·15), and 9 (pH 6·5).

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thus the cation (XVIII) lost principally the non-bonded proton. The low basicity of 1-methylpyrid-2-one sulphonylimine presumably arises from steric effects which are unfavourable for cation formation. pK_a values of the sulphonamido-compounds as acids are also recorded in Table 1; the 3-isomer is a somewhat stronger acid than the other two compounds because it exists mainly in the sulphonamido-form.

FIGS. 1—4.

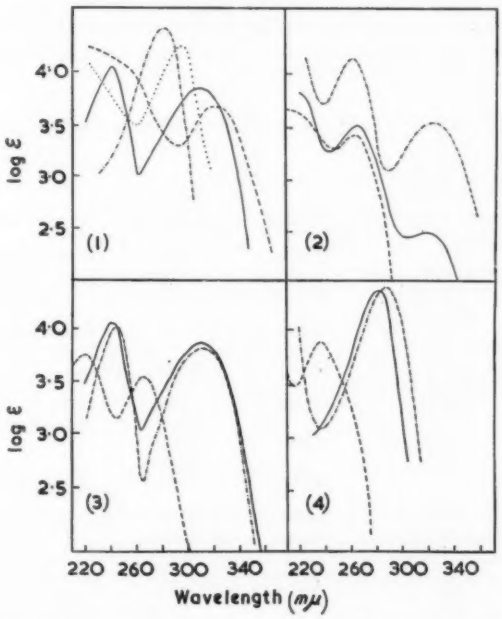

FIG. 1. —— *2-Methanesulphonamidopyridine at* pH 4·6. – – – *2-Toluene*-p-*sulphonamidopyridine in* 95% *ethanol*. — · — · — *4-Methanesulphonamidopyridine at* pH 6·5. . . . *4-Toluene*-p-*sulphonamidopyridine in* 95% *ethanol*.

FIG. 2. —— *3-Methanesulphonamidopyridine at* pH 5·15. – – – *3-(N-Methylmethanesulphonamido)-pyridine at* pH 10. — · — · — *Anhydro-3-methanesulphonamido-1-methylpyridinium hydroxide in* N-NaOH.

FIG. 3. —— *2-Methanesulphonamidopyridine at* pH 4·6. – – – *2-(N-Methylmethanesulphonamido)-pyridine at* pH 10. — · — · — *1-Methylpyrid-2-one methanesulphonylimine at* pH 10.

FIG. 4. —— *4-Methanesulphonamidopyridine at* pH 6·5. – – – *4-(N-Methylmethanesulphonamido)-pyridine at* pH 10. — · — · — *1-Methylpyrid-4-one methanesulphonylimine at* pH 10.

Ultraviolet Spectra (Table 2).—In each series, the spectra of the cations are similar, indicating their similar structure. For the 4-series, the spectrum of the potentially tautomeric compound closely resembles that of the fixed imine. It can be seen (Fig. 4) that *ca.* 3% of the other tautomeric form would be difficult to detect by this method.

For the 3-series (Fig. 2) the spectrum of the potentially tautomeric compound resembles that of the exocyclic *N*-methyl compound, but absorption is found in the 325 mμ region and calculation indicates a ratio of *ca.* 9 : 1 of pyridine to betaine structure.

For the 2-series (Fig. 3) the spectrum of the potentially tautomeric compound shows that it exists largely in the imino-form, but some absorption is found in the 265 mμ region which indicates *ca.* 10% may be present in the sulphonamidopyridine form.

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Infrared Spectra.—The infrared spectra of crystalline 2- and 4-methanesulphonamidopyridine closely resemble those of the corresponding 1-methylpyrid-2- and -4-one methanesulphonylimines and show distinct differences from those of the *N*-methylmethanesulphonamido-compounds.[10] The spectra of the imino-compounds are given in Table 3, with tentative assignments based on previous work.[10,13] The band near 1640 cm.$^{-1}$ is assigned to a ring mode; many pyridones and pyridthiones show a ring mode considerably above 1600 cm.$^{-1}$.[13] The spectrum of the deuterated derivative (XIX) differed most from that of the non-deuterated compound in the 1600—1500 cm.$^{-1}$ region where bands at 1563, 1528, and 1503 cm.$^{-1}$ appear in place of the shoulder at 1619 cm.$^{-1}$ and band at 1534 cm.$^{-1}$. Thus, an NH deformation mode presumably lies in this region, but as the *N*-methyl compounds

TABLE 3. *Infrared spectra of sulphonamidopyridines.*

2-Series			4-Series		
1-Methyl [a]		Potential tautomer [b]	1-Methyl [c]	Potential tautomer [b]	Tentative assignment
ν (cm.$^{-1}$)	ε_A	ν (cm.$^{-1}$)	ν (cm.$^{-1}$)	ν (cm.$^{-1}$)	
1643	340	1636s	1644vs	1636s	Ring stretch
1556	190	1620*s		1615m	νC=N and NH def?
1521	340	1535m	1515vs		
1470*	45	1465m			Ring stretch
1454	145	1430w	1436m		
1418	15				
1376	195	1394s	1380vs	1352s	
		1365s			
1323	115	1331m	1320m	1337s	SO_2 sym. stretch also one ring mode and one βCH
1287	100	1291s		1312s	
1265	220	1271s	1258s	1281m	
		1250s		1273m	
1189	45		1197s	1192m	βCH or Me rock
1176	30	1165w			
1122*	250	1119vs	1115*s	1116s	SO_2 asym. stretch
1110	400	1100*m	1104vs	1095*m	
1062	35				?
1030	30	1037m	1027m	1017w	N–S stretch
		997s		994w	Ring breathing
967	300	970s	965vs	966m	C–S stretch
		945m	939s		?
			832s	828w	γCH
807	115	803s			?

[a] Measured as a 0·189M-solution in $CHCl_3$ in a 0·106 mm. cell. [b] Nujol mull. Satd. solution in $CHCl_3$ in a 0·106 mm. cell. * Shoulder.

also absorb strongly here the νC=N vibrational frequency is also assigned to this region. The asymmetric SO_2 stretching vibration is at frequencies lower than those (1158—1146 cm.$^{-1}$) for sulphonamido-compounds;[10] for 1-methylpyrid-2-one methanesulphonylimine this band showed the expected shift towards lower frequencies as the proton-donor ability of the solvent increased.[14] All the compounds showed several strong bands in the 1400—1250 cm.$^{-1}$ region; the solvent shift method did not clearly indicate which were due to the SO_2 symmetric stretching mode. The band at 970—965 cm.$^{-1}$ is tentatively assigned to the C–S stretching mode; similar bands were found for the sulphonamido-compounds.[10] The N–S stretching vibrational mode is probably at 1037—1017 cm.$^{-1}$; its position could be considerably different from that (912—866 cm.$^{-1}$) found for sulphonamido-compounds.[10]

Discussion.—The above results indicate that, in aqueous solution, K_{imino}/K_{amino} = *ca.* 10, 0·1, and 30 in the 2-, 3-, and 4-series respectively. By using the pK_a values of Table 1,

[13] Katritzky and Jones, *J.*, 1960, 2947.
[14] Bellamy and Williams, *Trans. Faraday Soc.*, 1959, **55**, 14.

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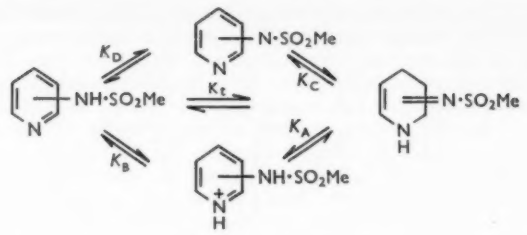

and following Mason,[15] the pK_a values for the individual tautomers can now be calculated (cf. scheme):

	pK_A	pK_B	pK_C	pK_D
2-Series	1·1	2·1	8·0	7·0
3-	4·5	3·5	6·0	7·0
4-	3·6	5·1	9·1	7·6

For the imino-compounds, the strength as acids (K_C) decreases in the order 3- > 2- > 4-substituted, and as bases (K_A) in the order 3- > 4- > 2-. The zwitterion would be expected to be the strongest, both as an acid and as a base, because the zwitterionic species is intrinsically less stable. Of 2- and 4-analogues, the proximity of the two nitrogen atoms in the 2-compound makes it the stronger acid and the weaker base.

For the amino-compounds as bases (K_B), the effect of the NH·SO_2Me group appears to be mainly inductive because the order is 4- > 3- > 2-. For the compounds as acids (K_D) the order is 2- ~ 3- > 4-, which again indicates inductive interaction although the 3-derivative is a surprisingly strong acid.

Experimental

2-Methanesulphonamidopyridine.—Methanesulphonyl chloride (1·15 g.) was added dropwise to 2-aminopyridine (0·94 g.) in pyridine (1·25 c.c.) at 0°. After 24 hr. at 20°, the mixture was added to water (3 c.c.); the resulting sulphonamide (1·25 g., 72%) crystallised from water in needles, m. p. 203—204° (lit.,[6] m. p. 204—206°) (Found: C, 41·9; H, 4·7; N, 16·2. Calc. for $C_6H_8N_2O_2S$: C, 41·9; H, 4·7; N, 16·3%).

1-Methylpyrid-2-one Methanesulphonylimine.—(*a*) 2-Methanesulphonamidopyridine (1·0 g.) and dimethyl sulphate (0·8 g.) in acetone (37 c.c.) were refluxed over potassium carbonate (1·7 g.) for 2 hr. Insoluble material was filtered off and the filtrate was evaporated. The residue was taken up in benzene and boiled with carbon. Evaporation then gave the *sulphonylimine* (0·35 g., 32%) which crystallised from chloroform in needles, m. p. 142·5—144° (lit.,[6] m. p. 146—147°, no analysis given) (Found: C, 45·3; H, 5·7; N, 15·3. $C_7H_{10}N_2O_2S$ requires C, 45·2; H, 5·4; N, 15·1%).

(*b*) 2-Amino-1-methylpyridinium iodide (1·4 g.) in methanol (3 c.c.) was shaken with silver oxide (0·69 g.). After filtration and evaporation, the residue was treated with pyridine (1·0 c.c.) and methanesulphonyl chloride (0·7 g.). After 2 hr., water (2 c.c.) was added and the whole extracted with chloroform (10 c.c.). Evaporation of the extracts gave 1-methylpyrid-2-one methanesulphonylimine (0·28 g., 25%), m. p. and mixed m. p. 139—140°. The infrared spectrum was identical with that of material prepared above.

(*c*) Diazomethane (*ca.* 3 g. in 100 c.c. of ether) was added dropwise and with agitation to 2-methanesulphonamidopyridine (5·8 g.) in methanol (150 c.c.). After 30 min., volatile material was removed at 100°/20 mm. The residue was extracted with ether (*A*). The residual 1-methylpyrid-2-one methanesulphonylimine (0·28 g., 25%), crystallised from chloroform, had m. p. and mixed m. p. 138—139°.

2-(N-Methylmethanesulphonamido)pyridine.—The ethereal extracts (*A*) above, on evaporation, gave the *pyridine* (4·4 g., 71%), b. p. 130—135° (bath)/0·1 mm., n^{23} 1·5370 (Found: C, 45·5; H, 5·6; N, 14·9. $C_7H_{10}N_2O_2S$ requires C, 45·2; H, 5·4; N, 15·1%).

3-Methanesulphonamidopyridine.—Methanesulphonyl chloride (1·2 g.) and 3-aminopyridine

[15] Mason, *J.*, 1958, 674.

(1·0 g.) were heated for 3 hr. at 100° in pyridine (1·3 c.c.). Addition of water (3 c.c.) gave the *sulphonamide* (1·6 g., 89%) which crystallised from water in plates, m. p. 140—141° (Found: C, 41·8; H, 4·8; N, 16·2%).

3-(N-*Methylmethanesulphonamido*)*pyridine*.—Ethereal diazomethane (*ca.* 0·5 g. in 25 c.c.) was added with agitation to 3-methanesulphonamidopyridine (1·0 g.) in methanol (25 c.c.) to give the *sulphonamide* (0·5 g., 45%) which distilled at 145—150° (bath)/0·06 mm. and solidified to plates, m. p. 62° (from ethanol) (Found: C, 45·1; H, 5·5; N, 14·9%).

3-*Methanesulphonamido*-1-*methylpyridinium Perchlorate*.—3-Methanesulphonamidopyridine (0·4 g.) and methyl toluene-*p*-sulphonate (0·44 g.) were kept at 120° for 10 hr. Cooling, and addition of 60% perchloric acid (1·0 c.c.), gave the *perchlorate* (0·4 g., 60%) which separated from ethanol as needles, m. p. 165·5—167° (Found: C, 29·8; H, 4·1; N, 10·1. $C_7H_{11}ClN_2O_6S$ requires C, 29·4; H, 3·9; N, 9·8%).

4-*Methanesulphonamidopyridine*.—4-Aminopyridine (2 g.) was refluxed with methanesulphonyl chloride (2·43 g.) in toluene (25 c.c.) for 2 hr. After cooling, the toluene was decanted from the oil, which, on being rubbed with ethanol (10 c.c.), solidified to give 4-*methanesulphonamidopyridine hydrochloride* (1·1 g., 25%), m. p. 251—253° (decomp.) (Found: C, 34·6; H, 4·5; N, 13·3. $C_6H_9ClN_2O_2S$ requires C, 34·5; H, 4·4; N, 13·4%). The hydrochloride (0·9 g.) in water (2 c.c.) was brought to pH 6·3 by 0·1N-sodium hydroxide. Continuous extraction with chloroform gave 4-*methanesulphonamidopyridine* (0·5 g., 66%), plates (from ethanol), m. p. 203—204° (Found: C, 41·4; H, 5·0; N, 16·3%).

1-*Methylpyrid*-4-*one Methanesulphonylimine and* 4-(N-*Methylmethanesulphonamido*)*pyridine*.—4-Methanesulphonamidopyridine hydrochloride (1·1 g.) under ethanol (20 c.c.) was shaken with excess of ethereal diazomethane. The resulting homogeneous mixture was evaporated and the oily residue extracted with ether. 1-*Methylpyrid*-4-*one methanesulphonylimine* (0·2 g., 20%) remained as an insoluble residue, m. p. 175·5—176° (from ethanol) (Found: C, 45·5; H, 5·3; N, 15·2%). The ethereal solution afforded 4-(N-*methylmethanesulphonamido*)*pyridine* (0·05 g., 5%), plates [from light petroleum (60—80°)], m. p. 53° (Found: C, 44·9; H, 5·7%).

This work was carried out during the tenure (by R. A. J.) of a D.S.I.R. grant.

University Chemical Laboratory, Cambridge. [*Received, July 20th*, 1960.]

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68. *Carcinogenic Nitrogen Compounds. Part XXIX.*[1] 2,5-*Diethylaniline and Benzacridines derived therefrom.*

By Michèle Marty, Ng. Ph. Buu-Hoï, and P. Jacquignon.

o-Ethylacetanilide is shown to undergo Friedel–Crafts acetylation with aluminium chloride and acetyl chloride in the position *para* to the ethyl group, thus providing a novel route to 2,5-diethylaniline; this last amine was used for the synthesis of new nitrogen-containing heterocyclic compounds, including several polysubstituted benzacridines. With acetic anhydride and zinc chloride, acetylation of *o*-ethylacetanilide took place in the position *meta* to the ethyl group.

In the Friedel–Crafts acetylation of *o*-methylacetanilide, using aluminium chloride as catalyst, the acetyl group enters the position *para* to the methyl group,[2] and as both theory and practice ascribe a lesser *ortho* : *para*-directing influence to the ethyl than to the methyl group,[3] it was of interest to investigate the behaviour of *o*-ethylacetanilide in the same reaction. The aluminium chloride-catalysed acetylation of *o*-ethylacetanilide with acetyl chloride was found to give, in low yield, 3-acetamido-4-ethylacetophenone (I), whose constitution was established by Huang-Minlon reduction of the corresponding amino-ketone to a substance identical with 2,5-diethylaniline (II) prepared from *p*-diethylbenzene

[1] Part XXVIII, Buu-Hoï, Périn, and Jacquignon, *J.*, 1960, 4500.
[2] Buu-Hoï, Ekert, and Royer, *Compt. rend.*, 1951, **233**, 627.
[3] See general discussion in Badger, "Structures and Reactions of the Aromatic Compounds," Cambridge Univ. Press, 1954.

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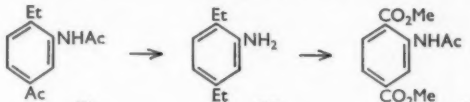
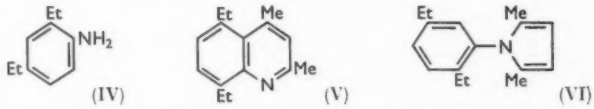
by nitration and reduction. This amine gave an *N*-acetyl derivative, m. p. 158·5°, whereas Voswinkel [4] gave m. p. 99° for 2,5-diethylacetanilide; a similar discrepancy was noted between the m. p. of our *N*-benzoyl derivative (107°) and that reported by von Auwers,

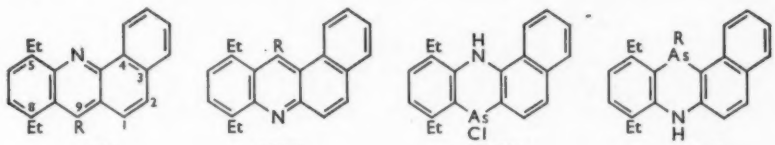


Lechner, and Bundesmann [5] for 2,5-diethylbenzanilide (*ca.* 130°). Hence it was thought useful to confirm the structure of our diethylaniline, and this was achieved by oxidising the *N*-acetyl derivative with potassium permanganate and working up the product to



dimethyl 2-acetamidoterephthalate (III), a substance already prepared by other routes.[6] Thus, the aluminium chloride-catalysed Friedel–Crafts acetylation of *o*-ethylacetanilide follows the same pattern as that of *o*-methylacetanilide. When, however, zinc chloride and acetic anhydride were used for the acetylation, substitution occurred, not in the position *para* to the ethyl group, but in the *meta* position, as Wolff–Kishner reduction yielded 2,4-diethylaniline (IV), identical with the amine obtained from *m*-diethylbenzene by nitration and reduction.[7] This is in line with Klingel's observation on the zinc chloride-catalysed acetylation of *o*-methylacetanilide by acetic anhydride.[8]

2,5-Diethylaniline was converted into various nitrogen-bearing heterocyclic compounds, for testing as potential carcinogens or cocarcinogens. A Combes–Beyer reaction [9] with acetylacetone, followed by cyclisation of the product with sulphuric acid, led to 5,8-diethyl-2,4-dimethylquinoline (V); condensation with hexane-2,5-dione yielded 1-(2,5-diethylphenyl)-2,5-dimethylpyrrole (VI). In the benzacridine series, 5,8-diethyl-3,4-benzacridine (VII; R = H) was synthesised by reaction with α-naphthol in the presence of paraformaldehyde; [10] and a similar reaction with β-naphthol afforded 5,8-diethyl-1,2-benzacridine (VIII; R = H). Knoevenagel condensation of α-naphthol with the amine (II)



in the presence of iodine [11] furnished *N*-(2,5-diethylphenyl)-α-naphthylamine; modified Bernthsen reactions [12] of this secondary amine with acetic and propionic anhydride gave respectively 5,8-diethyl-9-methyl- (VII; R = Me) and 5,8,9-triethyl-3,4-benzacridine (VII; R = Et), whose structures resembled those of homologues already found carcinogenic.[13]

[4] Voswinkel, *Ber.*, 1889, **22**, 315.
[5] von Auwers, Lechner, and Bundesmann, *Ber.*, 1925, **58**, 48.
[6] Ullmann and Uzbachian, *Ber.*, 1903, **36**, 1804.
[7] Copenhaver and Emmet Reid, *J. Amer. Chem. Soc.*, 1927, **49**, 3161.
[8] Klingel, *Ber.*, 1885, **18**, 2696.
[9] Combes, *Compt. rend.*, 1888, **106**, 1536; Beyer, *Ber.*, 1887, **20**, 1767.
[10] Ullmann and Fetvadjian, *Ber.*, 1903, **36**, 1029; Buu-Hoï, *J.*, 1950, 1146.
[11] Knoevenagel, *J. prakt. Chem.*, 1914, **89**, 17.
[12] Buu-Hoï and Lecocq, *Compt. rend.*, 1944, **218**, 792; Buu-Hoï, *J.*, 1946, 792.
[13] Cf. Lacassagne, Buu-Hoï, Daudel, and Zajdela, *Adv. Cancer Res.*, 1956, **4**, 315.

When β-naphthol was used in the Knoevenagel condensation of the amine (II), *N*-(2,5-diethylphenyl)-β-naphthylamine was obtained, from which 5,8-diethyl-9-methyl- (VIII; R = Me) and 5,8,9-triethyl-1,2-benzacridine (VIII; R = Et) were prepared.

In the phenarsazine series, 10-chloro-6,9-diethyl-5,10-dihydro-3,4- (IX) and -1,2-benzophenarsazine (X; R = Cl) were prepared by the Wieland–Rheinheimer reaction [14] of arsenic trichloride and the appropriate secondary amines; a dimethyl homologue of (IX) had already been found to produce papillomas of the skin in mice.[15] With methylmagnesium iodide, compound (X; R = Cl) yielded 6,9-diethyl-5,10-dihydro-10-methyl-1,2-benzophenarsazine (X; R = Me).

The results of biological investigation of these various compounds will be reported later.

Experimental

Aluminium Chloride-catalysed Acetylation of o-*Ethylacetanilide.*—This compound (199 g.), b. p. 178°/12 mm., m. p. 110°, was prepared from *o*-ethylaniline (b. p. 110°/12 mm.; 160 g.) and acetic anhydride (141·5 g.) in benzene (300 c.c.) by one hour's refluxing. To a suspension of this amide (100 g.) in anhydrous carbon disulphide (750 c.c.) and acetyl chloride (48 g.), powdered aluminium chloride (122·5 g.) was added in small portions, and the mixture refluxed for 10 hr. on a water-bath. After cooling and treatment with cold dilute hydrochloric acid, the product was taken up in chloroform, the organic layer was washed with aqueous sodium hydroxide, then with water, and dried (Na_2SO_4), the solvents were distilled off, and the residue was fractionated *in vacuo*. 3-*Acetamido*-4-*ethylacetophenone* (I) (33·5 g.) formed yellow crystals (from cyclohexane), m. p. 97°, b. p. 220°/15 mm. (Found: C, 70·0; H, 7·4. $C_{12}H_{15}NO_2$ requires C, 70·2; H, 7·3%). The 25% yield thus obtained was the highest in a series of experiments using various solvents and different periods of heating; with methylene chloride as solvent, no reaction took place, and only an 8% yield was recorded when light petroleum was used.

3-*Amino*-4-*ethylacetophenone.*—A mixture of the foregoing acetamido-ketone (37 g.) and hydrochloric acid (300 c.c.) was refluxed for 75 min.; after cooling and basification with aqueous sodium hydroxide, the *product* was taken up in ether and worked up in the usual way, giving a viscous yellow oil (18 g.), b. p. 187°/15 mm. (Found: N, 8·6. $C_{10}H_{13}NO$ requires N, 8·5%).

2,5-*Diethylaniline* (II).—A solution of the foregoing amino-ketone (25 g.) and hydrazine hydrate (15 g.) in diethylene glycol (300 c.c.) was refluxed for 6 hr. with potassium hydroxide (25 g.) under removal of water. After cooling and dilution with water, the product was taken up in benzene, the benzene solution dried (Na_2SO_4), the solvent distilled, and the residue fractionated *in vacuo*, giving a pale yellow oil (17 g.), b. p. 122°/15 mm., $n_D^{26\cdot3}$ 1·5418. Acetylation with acetic anhydride in benzene yielded 2,5-diethylacetanilide, m. p. 158·5° (from benzene) (Found: C, 75·3; H, 8·7. Calc. for $C_{12}H_{17}NO$: C, 75·4; H, 8·9%); Gaudion, Hook, and Plant [16] gave m. p. 154°, and Voswinkel [4] gave m. p. 99°. The *N*-benzoyl derivative of 2,5-diethylaniline crystallised from hexane as prisms, m. p. 107° (Found: C, 80·5; H, 7·8; N, 5·5. Calc. for $C_{17}H_{19}NO$: C, 80·6; H, 7·6; N, 5·5%) (lit.,[5] m. p. 130°). The *toluene*-p-*sulphonyl derivative* formed needles, m. p. 103°, from hexane (Found: N, 4·7. $C_{17}H_{21}NO_2S$ requires, N4·6%); the *methanesulphonyl derivative* formed leaflets, m. p. 76°, from hexane (Found: N, 5·9. $C_{11}H_{17}NO_2S$ requires N, 6·2%). The derivatives prepared from a sample of 2,5-diethylaniline synthesised by nitration of *p*-diethylbenzene and subsequent reduction had the same properties.

Oxidation of 2,5-*Diethylacetanilide.*—To a suspension of this compound (10 g.) in water (750 c.c.), potassium permanganate (70 g.) was added in small portions with stirring, and the mixture heated at 95° for 8 hr. and filtered. Acidification of the filtrate with hydrochloric acid furnished a precipitate of acetamidoterephthalic acid, which was deacetylated with hot hydrochloric acid; neutralisation gave aminoterephthalic acid, m. p. 325°, from water.[17] Esterification of this acid with methanol and sulphuric acid afforded dimethyl aminoterephthalate, crystallising as yellowish prisms, m. p. 135°, from ethanol (lit.,[18] m. p. 134°),

[14] Wieland and Rheinheimer, *Annalen*, 1921, **423**, 1.
[15] Lacassagne, Buu-Hoï, Royer, and Rudali, *Compt. rend. Soc. biol.*, 1951, **145**, 1451.
[16] Gaudion, Hook, and Plant, *J.*, 1947, 1631.
[17] Wegscheider, Perndanner, and Auspitzer, *Monatsh.*, 1910, **31**, 1299.
[18] Cahn-Speyer, *Monatsh.*, 1907, **28**, 805.

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which with acetic anhydride in benzene gave dimethyl acetamidoterephthalate, prisms, m. p. 168°, from benzene (lit.,[18] m. p. 167°).

Zinc Chloride-catalysed Friedel–Crafts Acetylation of o-*Ethylaniline.*—To a mixture of this amine (26 g.) and anhydrous zinc chloride (52 g.), acetic anhydride (104 g.) was cautiously added, and after 14 hours' refluxing the mixture was heated with hydrochloric acid for 90 min. After cooling and filtration, the filtrate was basified with sodium hydroxide, and the product taken up in benzene, washed with water and dried (Na_2SO_4), recovered, and fractionated *in vacuo*. The crude 4-amino-3-ethylacetophenone thus obtained as a yellow viscous oil (5·5 g.) was reduced with hydrazine hydrate and potassium hydroxide in diethylene glycol in the usual conditions, giving 2,4-diethylaniline (3 g.), b. p. 118—120°/24 mm.; the *N*-acetyl and the *N*-benzoyl derivative melted at 112° and 176° respectively (lit.,[7] 112—113·5° and 176·5°).

5,8-*Diethyl*-2,4-*dimethylquinoline* (V).—A mixture of 2,5-diethylaniline (4 g.) and acetylacetone (2·6 g.) was refluxed for 1 hr. with 1 drop of acetic acid, and the crude anil obtained was cyclised by sulphuric acid (3 parts) in 30 min. on a water-bath. After cooling, the mixture was basified with dilute aqueous sodium hydroxide, and the product taken up in ether, dried (Na_2SO_4), recovered, and fractionated *in vacuo*, giving the *quinoline* as a pale yellow oil (3·3 g.), b. p. 178—180°/15 mm., n_D^{21} 1·5792 (Found: N, 6·6. $C_{15}H_{19}N$ requires N, 6·6%); the *picrate* crystallised as golden-yellow leaflets, m. p. 133°, from ethanol (Found: N, 12·8. $C_{21}H_{22}N_4O_7$ requires N, 12·7%).

1-(2,5-*Diethylphenyl*)-2,5-*dimethylpyrrole* (VI).—A mixture of 2,5-diethylaniline (3 g.) and hexane-2,5-dione (3 g.) was refluxed for 2 hr. with 1 drop of acetic acid, then fractionated *in vacuo*, giving the *pyrrole* as a pale yellow oil (3·5 g.), b. p. 156°/20 mm. (Found: N, 5·9. $C_{16}H_{21}N$ requires N, 6·2%).

5,8-*Diethyl*-3,4-*benzacridine* (VII; R = H).—To a mixture of 2,5-diethylaniline (10 g.) and α-naphthol (10·6 g.), heated at *ca.* 250°, paraformaldehyde (7·2 g.) was cautiously added in small portions, and the product brought to the b. p. at atmospheric pressure, then fractionated *in vacuo*. The yellow resin obtained, b. p. >260°/20 mm., was dissolved in ethanol and converted into a *picrate*, which recrystallised from ethanol–benzene as yellow prisms, m. p. 141° (Found: N, 10·6. $C_{27}H_{22}N_4O_7$ requires N, 10·9%). Decomposition of this picrate with aqueous ammonia afforded the free *base* (0·8 g.), yellowish needles, m. p. 71° (from ethanol) (Found: C, 88·2; H, 6·7; N, 5·0. $C_{21}H_{19}N$ requires C, 88·4; H, 6·7; N, 4·9%).

5,8-*Diethyl*-1,2-*benzacridine* (VIII; R = H).—Similarly prepared from 2,5-diethylaniline (12 g.) and β-naphthol (12·7 g.) with paraformaldehyde (8·7 g.), this *acridine* crystallised as yellowish needles (1 g.), m. p. 109°, from ethanol (Found: C, 88·4; H, 6·6; N, 4·7%); the addition compound with picric acid formed golden-yellow needles, m. p. 245° (decomp. >208°), from ethanol–benzene.

N-(2,5-*Diethylphenyl*)-α-*naphthylamine*.—A mixture of 2,5-diethylaniline (7·5 g.) and α-naphthol (9·5 g.) was refluxed for 18 hr. with a few crystals of iodine; after cooling and treatment with aqueous sodium hydroxide, the *product* was taken up in ether, dried (Na_2SO_4), recovered, and fractionated *in vacuo*, giving a pale yellow oil (6 g.), b. p. 249—250°/13 mm. (Found: C, 87·1; H, 7·6; N, 5·2. $C_{20}H_{21}N$ requires C, 87·3; H, 7·6; N, 5·1%).

5,8-*Diethyl*-9-*methyl*-3,4-*benzacridine* (VII; R = Me).—A mixture of the foregoing secondary amine (13 g.), acetic anhydride (7·5 g.), and freshly fused zinc chloride (8 g.) was gently refluxed for 40 hr. After cooling and treatment with aqueous sodium hydroxide, the product was taken up in benzene, washed with water, dried (Na_2SO_4), recovered, and fractionated *in vacuo*, giving a yellow resin (8 g.), b. p. >260°/20 mm., which was dissolved in ethanol and converted into a *picrate*; this crystallised as deep yellow needles, m. p. 205° (decomp. >180°), from ethanol–benzene (Found: C, 63·9; H, 4·6. $C_{28}H_{24}N_4O_7$ requires C, 63·6; H, 4·5%). Basification with aqueous ammonia afforded the free *base*, as yellowish prisms, m. p. 88° (from hexane) (Found: C, 88·6; H, 6·9; N, 4·5. $C_{22}H_{21}N$ requires C, 88·3; H, 7·0; N, 4·7%).

5,8,9-*Triethyl*-3,4-*benzacridine* (VII; R = Et).—This was prepared as above from *N*-(2,5-diethylphenyl)-α-naphthylamine (15 g.), propionic anhydride (9·5 g.), and zinc chloride (9·2 g.); after the usual treatment, the portion of b. p. 270—278°/14 mm. (10·7 g.) was converted into a *picrate*, which formed deep yellow needles, m. p. 231°, from benzene (Found: C, 63·9; H, 4·5; N, 10·6. $C_{29}H_{26}N_4O_7$ requires C, 64·2; H, 4·8; N, 10·3%). The free *base* crystallised from hexane as yellowish needles, m. p. 92° (Found: C, 87·4; H, 7·0; N, 4·7. $C_{23}H_{23}N$ requires C, 87·2; H, 7·3; N, 4·5%).

N-(2,5-*Diethylphenyl*)-β-*naphthylamine*.—A mixture of 2,5-diethylaniline (20 g.) and β-naphthol (25 g.) was refluxed for 24 hr. with iodine (1 g.), and the product worked up in the usual

way, giving a viscous yellow oil (13 g.), b. p. 253°/23 mm. (Found: C, 87·2; H, 7·5%); the corresponding picrate crystallised as violet-brown needles, m. p. 90°, from cyclohexane.

5,8-*Diethyl*-9-*methyl*-1,2-*benzacridine* (VIII; R = Me).—Prepared from the foregoing secondary amine (13 g.), acetic anhydride (7·5 g.), and zinc chloride (8·7 g.), this *acridine*, b. p. 276°/18 mm., formed cream-coloured needles (2 g.), m. p. 144°, from ethanol (Found: C, 88·1; H, 5·7; N, 4·8%). Its *picrate* crystallised as golden-yellow needles, m. p. 242° (decomp. >205°), from benzene (Found: N, 10·9%).

5,8,9-*Triethyl*-1,2-*benzacridine* (VIII; R = Et).—Prepared from the secondary amine (11 g.), propionic anhydride (6·8 g.), and zinc chloride (6·5 g.), this *acridine*, even after purification *via* its picrate, did not crystallise and formed a yellow, viscous oil (2 g.), b. p. 275—280°/22 mm. (Found: C, 87·0; H, 7·5%).

10-*Chloro*-6,9-*diethyl*-5,10-*dihydro*-3,4-*benzophenarsazine* (IX).—A solution of *N*-(2,5-diethylphenyl)-α-naphthylamine (2 g.) and arsenic trichloride (1·3 g.) in dry *o*-dichlorobenzene (8 c.c.) was gently refluxed for 90 min.; the precipitate formed on concentration and cooling was recrystallised from chlorobenzene, giving golden-yellow leaflets (1·8 g.), m. p. 223° (decomp. >160°) (Found: N, 3·6. $C_{20}H_{19}AsClN$ requires N, 3·6%. No satisfactory carbon value could be obtained).

10-*Chloro*-6,9-*diethyl*-5,10-*dihydro*-1,2-*benzophenarazine* (X; R = Cl).—Similarly prepared from *N*-(2,5-diethylphenyl)-β-naphthylamine (4 g.) and arsenic trichloride (2·7 g.), this *compound* formed golden-yellow leaflets (4 g.), m. p. 229° (decomp. >200°), from chlorobenzene, giving brown-red solutions in sulphuric acid (Found: C, 62·6; H, 5·0; N, 3·8. $C_{20}H_{19}AsClN$ requires C, 62·6; H, 5·0; N, 3·6%). 6,9-*Diethyl*-5,10-*dihydro*-10-*methyl*-1,2-*benzophenarsazine* (X; R = Me), prepared from the foregoing chloro-derivative (1 g.) with a slight excess of methylmagnesium iodide in anhydrous ether, formed colourless needles (0·7 g.), m. p. 86°, from methanol and gave red solutions in sulphuric acid (Found: C, 69·1; H, 6·1. $C_{21}H_{22}AsN$ requires C, 69·4; H, 6·1%).

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THE RADIUM INSTITUTE, THE UNIVERSITY OF PARIS. [*Received, July 25th*, 1960.]

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69. *The Ionisation Constants of Some Substituted Anilines and Phenols: A Test of the Hammett Relation.*

By A. I. BIGGS and R. A. ROBINSON.

The ionisation constants of aniline and 21 substituted anilines, and of phenol and 13 substituted phenols, in aqueous solution at 25° have been measured by the spectrophotometric method. The Hammett ρ parameter is found to be 2·889 for the aniline series and 2·229 for the phenol series, these parameters predicting the ionisation constants of 26 *meta*- and *para*-substituted compounds with a mean deviation of 0·04 in pK.

THE ionisation constants of phenol, the cresols, nitrophenols, and methoxyphenols in aqueous solution at 25° have already been determined spectrophotometrically.[1] Measurements are now reported on the twelve halogenophenols and on the corresponding halogeno- and nitro-anilines, the toluidines, and the anisidines. The ionisation constant of *m*-nitrophenol has been redetermined in borax buffers which we believe to be more reliable than the barbitone buffer used previously. Data are now available for 28 *meta*- and *para*-substituted anilines and phenols and they can be used to test Hammett's relation:[2] $pK = \sigma\rho$, by using a set of σ values obtained by putting ρ = 1 for the substituted benzoic acids; with one exception, all the σ values needed can be got from the conductance measurements of Dippy *et al.*;[3] the remaining acid, *p*-iodobenzoic acid, has been studied

[1] Biggs, *Trans. Faraday Soc.*, 1954, **50**, 800; 1956, **52**, 35; Robinson and Biggs, *ibid.*, 1955, **51**, 901.
[2] Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940.
[3] Dippy and Williams, *J.*, 1934, 1888; Dippy, Williams, and Lewis, *J.*, 1935, 343; Dippy and Lewis, *J.*, 1936, 644; 1937, 1426.

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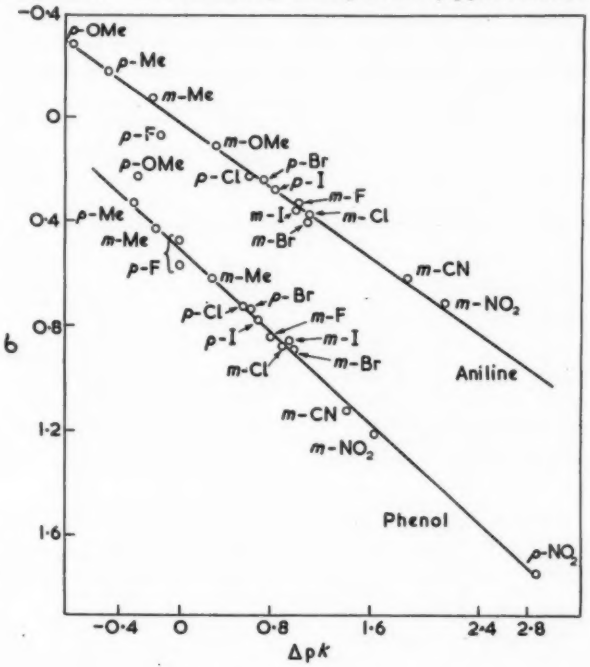
recently.[4] It is hoped that the present work, in which all the ionisation constants are measured by the same method, will provide a useful supplement to Jaffe's recent survey[5] of Hammett's relation.

Table 1 contains the results of the measurements on the substituted anilines and phenols, together with those obtained previously for phenol, the cresols, methoxyphenols,

*p*K *of substituted anilinium ions and phenols versus* σ. *The* σ*-scale is displaced 0·5 to the right in plotting points for the substituted phenols. The* σ*-values are derived from* p*K data for substituted benzoic acids except for* p*-nitrophenol and* p*-nitroaniline for which* σ = 1·239 *is used and for* p*-fluorophenol where two points are plotted, one on the right with* σ = 0·062 *derived from the* p*K value of* p*-fluorobenzoic acid and one on the left with* σ = −0·026 *derived from the* p*K value of* p*-fluoroaniline.*



and *o*- and *p*-nitrophenol. For the anilines, it is the acid ionisation constant which is given, *i.e.*, that of the acid conjugate to the substituted aniline. It is hoped that the results are accurate to the second decimal place but it is difficult to know if this has been achieved; we have found in the literature fifty p*K* values recorded which agree within 0·06 with those given in Table 1, the mean difference being 0·02, but it is not always possible to decide if it is the thermodynamic ionisation constant which has been reported and to what extent liquid-junction potentials have affected p*K* values derived from glass-electrode measurements.

A graph of Δp*K* of the substituted anilinium ions, *i.e.*, p*K* (anilinium ion) − p*K* (substituted anilinium ion), against Δp*K* of the substituted benzoic acids is given in the Figure. Twelve of the points lie close to a straight line, the exceptions being *p*-nitroaniline (not shown on the graph) and *p*-fluoroaniline. The equation of the best straight line through the points is p$K = 0{\cdot}023 + 2{\cdot}889\sigma$, so that the best value of the ρ parameter for the anilinium series is 2·889 and the p*K* values of substituted anilines can be represented by

[4] Robinson and Ang, *J.*, 1959, 2314.
[5] Jaffé, *Chem. Rev.*, 1953, **53**, 191.

$pK = 4{\cdot}580 - 2{\cdot}889\sigma$, with a mean difference of 0·04 between observed and calculated values.

In the phenol series, as the Figure shows, twelve points lie close to a straight line, the value of $\sigma(p\text{-}NO_2)$ being taken from the aniline series. The equation of the best straight line through the points is $pK = 0{\cdot}079 + 2{\cdot}229\sigma$, so that the best value of the ρ parameter for the phenol series is 2·229 and the pK values of substituted phenols can be represented by $pK = 9{\cdot}919 - 2{\cdot}229\sigma$, with a mean difference of 0·04 between observed and calculated values. *m*-Cyanoaniline and *m*-cyanophenol have been reported [6] to have pK 2·746 and 8·608 respectively; the above equations predict 2·783 and 8·550, $\sigma(m\text{-CN}) = 0{\cdot}614$ being used from the measurements of Briegleb and Bieber.[7]

There are, however, some anomalies which can be demonstrated by using the experimental data to calculate σ with $\rho = 1$, 2·889, and 2·229 in the benzoic acid, aniline, and phenol series respectively; the following σ values are calculated for four *para*-substituents:

	Benzoic acid	Aniline	Phenol
p-NO_2	0·778	1·239	1·243
p-OMe	−0·268	−0·264	−0·130
p-F	0·062	−0·026	0·005
p-CN	0·671	0·983	0·874

TABLE 1. pK *Values of substituted aniline and phenols at* 25°.

	o	*m*	*p*		*o*	*m*	*p*
Aniline		(4·60)		Phenol		(10·00)	
Fluoroaniline	3·20	3·59 (+1)	4·65	Fluorophenol	$8{\cdot}70_5$	9·21 (−4)	9·91
Chloroaniline	2·65	3·52 (−2)	3·98 (−5)	Chlorophenol	8·53	9·13 (−4)	9·42 (0)
Bromoaniline	2·53	3·58 (−8)	3·86 (+5)	Bromophenol	8·44	9·03 (+2)	9·36 (+4)
Iodoaniline	2·60	3·61 (−4)	3·78 (+1)	Iodophenol	8·51	9·06 (+7)	$9{\cdot}30_5$ (0)
Toluidine	4·45	4·73 (+5)	5·08 (0)	Cresol	10·29	10·09 (−2)	10·26 (+4)
Anisidine	4·52	4·23 (+1)	5·34 (+1)	Methoxyphenol	9·98	9·65 (+1)	10·21
Nitroaniline	−0·26	2·46 (+7)	1·00	Nitrophenol	7·21	$8{\cdot}38_5$ (−5)	7·15 (+1)

The figures in parentheses give the difference in pK ($\times 10^3$) between the observed value and that calculated by: $pK = 4{\cdot}580 - 2{\cdot}889\sigma$ for substituted anilinium ions, and $pK = 9{\cdot}919 - 2{\cdot}229\sigma$ for substituted phenols, the difference being recorded as positive if the calculated value is greater than the observed.

TABLE 2. *Buffer solutions.*

Solution		pH	$-\log \gamma_1$
Formate buffer: xM-$H{\cdot}CO_2H$ + 1·247xM-$H{\cdot}CO_2K$ + 1·079xM-KCl (see ref. *a*)			
Formate A	$x = 0{\cdot}025$	3·77	0·087
Formate B	$x = 0{\cdot}010$	3·80	0·063
Acetate buffer: xM-$C_2H_4O_2$ + xM-$C_2H_3O_2Na$ (see ref. 9)			
Acetate A	$x = 0{\cdot}1$	4·66	0·102
Acetate B	$x = 0{\cdot}05$	4·68	0·083
Acetate C	$x = 0{\cdot}01$	4·72	0·044
Succinate buffer: xM-$C_4H_5O_4Na$ + xM-$C_4H_4O_4Na_2$ (see ref. *b*)			
Succinate A	$x = 0{\cdot}05$	5·34	0·117
Succinate B	$x = 0{\cdot}025$	5·40	0·102
Succinate C	$x = 0{\cdot}01$	5·47	0·077
Borax buffer: 50 ml. 0·025M-borax + x ml. 0·1M-HCl diluted to 100 ml. (see ref. *c*)			
Borax A	$x = 16{\cdot}6$	8·40	0·065
Borax B	$x = 15{\cdot}2$	8·50	0·065
Borax C	$x = 13{\cdot}5$	8·60	0·065
Borax D	$x = 11{\cdot}6$	8·70	0·065
Borax E	$x = 9{\cdot}4$	8·80	0·065
Borax F	$x = 7{\cdot}1$	8·90	0·065
Borax buffer: 50 ml. 0·025M-borax + x ml. 0·1M-NaOH diluted to 100 ml. (see ref. *c*)			
Borax G	$x = 15{\cdot}0$	9·80	0·077
Borax H	$x = 16{\cdot}7$	9·90	0·078
Borax I	$x = 18{\cdot}3$	10·00	0·079
Borax buffer (see ref. *b*)			
0·025M-Borax		9·17	0·083
0·05M-Borax		9·20	0·102
Carbonate buffer (see ref. *b*)			
0·025M-$NaHCO_3$ + 0·025M-Na_2CO_3		10·02	0·102

[a] Calc. from data of Harned and Embree (*J. Amer. Chem. Soc.*, 1934, **56**, 1042). [b] Manov, DeLollis, Lindvall, and Acree, *J. Res. Nat. Bur. Stand.*, 1946, **36**, 543; Bates, Pinching, and Smith, *ibid.*, 1950, **45**, 418. [c] Bates and Bower, *ibid.*, 1955, **55**, 197; *Analyt. Chem.*, 1956, **28**, 1322.

[6] Fickling, Fischer, Mann, Packer, and Vaughan, *J. Amer. Chem. Soc.*, 1959, **81**, 4226.
[7] Briegleb and Bieber, *Z. Elektrochem.*, 1951, **55**, 250.

TABLE 3. *Ionization constants at 25°.*

Aniline: $5{\cdot}3 \times 10^{-4}$N; 281 mμ; $D_1 = 0$; $D_2 = 0{\cdot}716$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Acetate A	0·338	−0·049	4·606
Acetate B	0·356	−0·005	4·606
Acetate C	0·400	0·102	4·598

o-Fluoroaniline: $3{\cdot}4 \times 10^{-4}$N; 277 mμ; $D_1 = 0$; $D_2 = 0{\cdot}550$

Solution	D	$\log \alpha/(1-\alpha)$	$-\log m_{H^+}$	pK
0·0025M-HCl	0·122	−0·545	2·651	3·196
0·0020M-HCl	0·147	−0·438	2·757	3·195
0·0015M-HCl	0·180	−0·313	2·896	3·209
0·0010M-HCl	0·238	−0·118	3·066	3·211

m-Fluoroaniline: $4{\cdot}5 \times 10^{-4}$N; 278 mμ; $D_1 = 0{\cdot}013$; $D_2 = 0{\cdot}662$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Formate A	0·375	0·101	3·594
Formate B	0·402	0·175	3·582

p-Fluoroaniline: $4{\cdot}5 \times 10^{-4}$N; 287 mμ; $D_1 = 0{\cdot}001$; $D_2 = 0{\cdot}809$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Acetate A	0·354	−0·104	4·660
Acetate B	0·377	−0·047	4·647

o-Chloroaniline: $3{\cdot}9 \times 10^{-4}$N; 285 mμ; $D_1 = 0{\cdot}002$; $D_2 = 0{\cdot}767$

Solution	D	$\log \alpha/(1-\alpha)$	$-\log m_{H^+}$	pK
0·005M-HCl	0·248	−0·324	2·325	2·649
0·004M-HCl	0·288	−0·224	2·425	2·649
0·003M-HCl	0·347	−0·085	2·555	2·640
0·002M-HCl	0·426	0·095	2·739	2·644

m-Chloroaniline: $3{\cdot}9 \times 10^{-4}$N; 287 mμ; $D_1 = 0{\cdot}004$; $D_2 = 0{\cdot}646$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Formate A	0·388	0·173	3·522
Formate B	0·412	0·242	3·515

p-Chloroaniline; $3{\cdot}9 \times 10^{-4}$N; 292 mμ; $D_1 = 0{\cdot}001$; $D_2 = 1{\cdot}100$; 2 cm. cells

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Formate A	0·375	−0·287	3·980
Formate B	0·413	−0·222	3·971

o-Bromoaniline: $2{\cdot}9 \times 10^{-4}$N; 287 mμ; $D_1 = 0{\cdot}003$; $D_2 = 0{\cdot}624$.

Solution	D	$\log \alpha/(1-\alpha)$	$-\log m_{H^+}$	pK
0·00318M-HCl	0·308	−0·015	2·518	2·533
0·00265M-HCl	0·337	0·066	2·599	2·533
0·00212M-HCl	0·372	0·166	2·699	2·533

m-Bromoaniline: $2{\cdot}9 \times 10^{-4}$N; 286 mμ; $D_1 = 0{\cdot}004$; $D_2 = 0{\cdot}524$.

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Formate A	0·313	0·166	3·527
Formate B	0·330	0·225	3·527

p-Bromoaniline: $2{\cdot}9 \times 10^{-4}$N; 291 mμ; $D_1 = 0{\cdot}000$; $D_2 = 0{\cdot}768$.

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Formate A	0·306	−0·179	3·870
Formate B	0·336	−0·109	3·857

o-Iodoaniline: $2{\cdot}3 \times 10^{-4}$N; 290 mμ; $D_1 = 0{\cdot}017$; $D_2 = 0{\cdot}548$.

Solution	D	$\log \alpha/(1-\alpha)$	$-\log m_{H^+}$	pK
0·00262M-HCl	0·295	0·041	2·600	2·559
0·00210M-HCl	0·325	0·140	2·698	2·558
0·00158M-HCl	0·361	0·265	2·824	2·559

m-Iodoaniline: $2{\cdot}3 \times 10^{-4}$N; 290 mμ; $D_1 = 0{\cdot}014$; $D_2 = 0{\cdot}477$.

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Formate A	0·265	0·073	3·618
Formate B	0·285	0·150	3·598

p-Iodoaniline: $4{\cdot}6 \times 10^{-4}$N; 290 mμ; $D_1 = 0{\cdot}030$; $D_2 = 0{\cdot}658$.

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Formate A	0·309	−0·097	3·791
Formate B	0·336	−0·022	3·777
(0·00106M-HCl)	0·154	−0·609	3·769

o-Toluidine: $4{\cdot}7 \times 10^{-4}$N; 281 mμ; $D_1 = 0{\cdot}005$; $D_2 = 0{\cdot}794$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Acetate A	0·448	0·107	4·450
Acetate B	0·467	0·150	4·451
Acetate C	0·512	0·255	4·445

m-Toluidine: $4{\cdot}7 \times 10^{-4}$N; 281 mμ; $D_1 = 0{\cdot}002$; $D_2 = 0{\cdot}644$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Acetate A	0·258	−0·178	4·734
Acetate B	0·274	−0·134	4·734
Acetate C	0·311	−0·032	4·715

p-Toluidine: $4{\cdot}7 \times 10^{-4}$N; 287 mμ; $D_1 = 0{\cdot}000$; $D_2 = 0{\cdot}674$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Acetate A	0·154	−0·529	5·084
Acetate B	0·168	−0·479	5·077
Acetate C	0·197	−0·384	5·068

o-Anisidine: 2×10^{-4}N; 282 mμ; $D_1 = 0{\cdot}054$; $D_2 = 0{\cdot}547$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Acetate A	0·309	0·030	4·526
Acetate B	0·322	0·076	4·522

m-Anisidine: 2×10^{-4}N; 283 mμ; $D_1 = 0{\cdot}050$; $D_2 = 0{\cdot}393$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Acetate A	0·281	0·314	4·242
Acetate B	0·291	0·373	4·226

p-Anisidine: $2{\cdot}9 \times 10^{-4}$N; 295 mμ; $D_1 = 0{\cdot}002$; $D_2 = 0{\cdot}601$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Succinate A	0·264	−0·019	5·338
Succinate B	0·287	−0·042	5·349
Succinate C	0·323	0·063	5·345

o-Nitroaniline: $1{\cdot}8 \times 10^{-4}$N; 418 mμ; $D_1 = 0{\cdot}000$; $D_2 = 0{\cdot}802$

Solution	D	$\log \alpha/(1-\alpha)$	$-$pK (apparent)
1·0M-HCl	0·446	0·098	0·098
0·9M-HCl	0·474	0·160	0·114
0·8M-HCl	0·504	0·228	0·131
0·7M-HCl	0·535	0·302	0·147
0·6M-HCl	0·567	0·383	0·161
0·5M-HCl	0·600	0·473	0·172
0·4M-HCl	0·638	0·590	0·192
0·3M-HCl	0·677	0·734	0·211
0·2M-HCl	0·717	0·926	0·227

pK (apparent) extrapolated to zero ionic strength = −0·263.

TABLE 3. (*Continued.*)

m-Nitroaniline: $3{\cdot}6 \times 10^{-4}$N; 360 mμ; $D_1 = 0{\cdot}038$; $D_2 = 0{\cdot}513$

Solution	D	$\log \alpha/(1-\alpha)$	$-\log m_{H^+}$	pK
0·0040M-HCl	0·266	−0·035	2·419	2·454
0·00262M-HCl	0·313	0·141	2·608	2·467
0·0025M-HCl	0·320	0·165	2·628	2·463
0·0021M-HCl	0·340	0·242	2·706	2·464
0·0020M-HCl	0·347	0·270	2·727	2·457

p-Nitroaniline: $7{\cdot}2 \times 10^{-5}$N; 382 mμ; $D_1 = 0{\cdot}002$; $D_2 = 0{\cdot}925$

Solution	D	$\log \alpha/(1-\alpha)$	pK (apparent)
0·1156M-HCl	0·421	−0·080	1·017
0·0779M-HCl	0·515	0·097	1·012
0·0516M-HCl	0·606	0·277	1·010

Phenol: a repetition of earlier work [1] using carbonate buffer at 280, 290, and 300 mμ confirms the value of pK 9·998.

o-Fluorophenol: $4{\cdot}5 \times 10^{-4}$N; 284 mμ; $D_1 = 0{\cdot}023$; $D_2 = 1{\cdot}005$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
Borax D	0·545	0·055	8·700
Borax E	0·596	0·147	8·710

m-Fluorophenol: $4{\cdot}5 \times 10^{-4}$N; 283 mμ; $D_1 = 0{\cdot}038$; $D_2 = 1{\cdot}107$

0·025M-Borax	0·603	0·050	9·202
0·050M-Borax	0·626	0·087	9·209

p-Fluorophenol: 2×10^{-4}N; 298 mμ; $D_1 = 0{\cdot}018$; $D_2 = 0{\cdot}598$

Borax G	0·295	−0·039	9·910
Borax H	0·328	0·060	9·911
Borax I	0·362	0·164	9·906
Carbonate	0·377	0·201	9·918

Similar measurements at 277 and 240 mμ give pK = 9·907 and 9·905 respectively.

o-Chlorophenol: $1{\cdot}9 \times 10^{-4}$N; 300 mμ; $D_1 = 0{\cdot}002$; $D_2 = 0{\cdot}593$

Borax B	0·310	0·037	8·522
Borax C	0·339	0·123	8·536
Borax D	0·372	0·224	8·535
Borax E	0·403	0·324	8·535
Borax F	0·429	0·416	8·543

m-Chlorophenol: $1{\cdot}9 \times 10^{-4}$N; 300 mμ; $D_1 = 0{\cdot}087$; $D_2 = 0{\cdot}480$

Buffer	D	$\log \alpha/(1-\alpha)$	pK
0·025M-Borax	0·312	0·127	9·126
0·050M-Borax	0·320	0·163	9·134

p-Chlorophenol: $1{\cdot}9 \times 10^{-4}$N; 300 mμ; $D_1 = 0{\cdot}010$; $D_2 = 0{\cdot}453$

0·025M-Borax	0·191	−0·161	9·415
0·050M-Borax	0·200	−0·124	9·421

o-Bromophenol: $2{\cdot}9 \times 10^{-4}$N; 296 mμ; $D_1 = 0{\cdot}002$; $D_2 = 1{\cdot}153$

Borax A	0·586	0·013	8·442
Borax B	0·653	0·115	8·440
Borax C	0·713	0·208	8·448

m-Bromophenol: $2{\cdot}9 \times 10^{-4}$N; 294 mμ; $D_1 = 0{\cdot}018$; $D_2 = 0{\cdot}462$

0·025M-Borax	0·297	0·228	9·024
0·050M-Borax	0·305	0·262	9·035

p-Bromophenol: $2{\cdot}9 \times 10^{-4}$N; 299 mμ; $D_1 = 0{\cdot}027$; $D_2 = 0{\cdot}663$

0·025M-Borax	0·308	−0·102	9·355
0·050M-Borax	0·320	−0·068	9·365

o-Iodophenol: $1{\cdot}2 \times 10^{-4}$N; 298 mμ; $D_1 = 0{\cdot}018$; $D_2 = 0{\cdot}489$

Borax B	0·268	0·054	8·506
Borax C	0·294	0·151	8·509

m-Iodophenol: $2{\cdot}3 \times 10^{-4}$N; 295 mμ; $D_1 = 0{\cdot}043$; $D_2 = 0{\cdot}756$

0·025M-Borax	0·480	0·200	9·053
0·050M-Borax	0·493	0·233	9·064

p-Iodophenol: $2{\cdot}3 \times 10^{-4}$N; 295 mμ; $D_1 = 0{\cdot}125$; $D_2 = 0{\cdot}504$

0·025M-Borax	0·304	−0·048	9·301
0·050M-Borax	0·312	−0·011	9·308

m-Nitrophenol: $3{\cdot}6 \times 10^{-4}$N; 420 mμ; $D_1 = 0{\cdot}008$; $D_2 = 0{\cdot}452$

Borax A	0·248	0·071	8·831
Borax B	0·272	0·166	8·389

Thus for *p*-NO_2 substitution the σ-value which holds for both the aniline and the phenol series does not hold in the benzoic acid series, whereas for *p*-OMe substitution the σ-value which is valid in both the benzoic acid and the aniline series does not hold in the phenol series. Again, three different σ-values are needed for *p*-CN substitution, whilst for *p*-F substitution, although the σ-values in the aniline and phenol series are not very far apart, they differ considerably from that in the benzoic acid series.

EXPERIMENTAL

Measurements were made with a "Uvispek" instrument in an air-conditioned room at 25° ± 0·05°; a few experiments were made to show that a change of 0·05° corresponds to a change of about 0·007 in pK. Unless otherwise mentioned in Table 1, measurements were made with 1 cm. cells. The anilines and phenols were the purest specimens obtainable; these were recrystallised from water wherever possible; otherwise, they were distilled in a stream of nitrogen at low pressure and the middle fractions taken. Table 2 lists the buffers used for the phenols and for those anilines with pK > 3·5; for the four *o*-halogenoanilines and the three nitrophenols, *i.e.*, the anilines with pK < 3·5, hydrochloric acid was added to the aniline solutions. The ionisation constants calculated from the experimental data proved independent

of the concentration of the buffer solution or of the concentration of hydrochloric acid added, except for *o*- and *p*-nitroaniline. *o*-Nitroaniline showed considerable variation in " apparent " pK with hydrochloric acid concentration, which is not surprising as the implicit assumption that log $\gamma_{H^+}/\gamma_{RNH^+} = 0$ is unlikely to be valid at the high concentrations of hydrochloric acid that had to be used; the " apparent " pK, however, varied linearly with acid concentration and could be extrapolated easily. The " apparent " pK of *p*-nitroaniline showed less variation with acid concentration.

Table 3 gives the experimental details, the symbols having the meaning given in previous papers.[4,5]

We acknowledge with gratitude the assistance of Professor R. L. Huang who provided us with purified specimens of *p*-fluorophenol and *m*-iodophenol.

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[5] Biggs, *J.*, 1956, 2485.

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70. *Molecular Complexes based on Derivatives of 4,4′-Dihydroxytriphenylmethane.*

By G. B. BARLOW and A. C. CLAMP.

Numerous derivatives of 4,4′-dihydroxytriphenylmethane have been shown to give rise to molecular complexes, the enclosed compounds being held in long channels in the crystals. From the size of molecule which can be included, the channels are believed to be 6 Å or more in diameter. Heats of formation have been measured in a number of cases. Polymerisation of isoprene in several clathrate complexes by γ-radiation did not give rise to stereoregular polymers.

THE formation and composition of some complexes between triphenylmethane derivatives and some aromatic compounds have been studied by Driver and his co-workers.[1,2] The one essential condition is that the triphenylmethane should have two hydroxyl groups in *para*-positions. A definite molecular ratio between the components was found in almost all cases, a situation normally associated with clathrate formation. On the basis of X-ray diffraction studies, Powell [3] has suggested that the triphenylmethane molecules form a layer-like structure whereby each hydroxyl group is hydrogen-bonded to hydroxyl groups from two other molecules; the substituent on the third phenyl group is " sterically linked " to the corresponding group in another molecule, *i.e.*, forms an interlocking assembly.

Under suitable conditions, it has been found possible to prepare channel complexes. Their formation and properties are described below.

EXPERIMENTAL

The 4,4′-dihydroxytriphenylmethanes were prepared as described by Driver,[1,2] the appropriate benzaldehyde being condensed with a slight excess of a phenol in the presence of acetic acid–sulphuric acid. After being washed free from acid, they were recrystallised from benzene, giving rise to the benzene complex. The unsolvated 4,4′-dihydroxytriphenylmethane was obtained by heating these complexes *in vacuo* to constant weight.

The annexed Table 1 lists the triphenylmethanes prepared and some of their properties. Channel complexes were formed by mixing the free compound with an excess of the other component in the presence of absolute methyl alcohol (*ca.* 5% based on the triphenylmethane). Complex-formation was usually complete in 24—48 hr., the extent of the inclusion being measured by X-ray powder photographs. The second components used were straight-chain,

[1] Driver and Mok, *J.*, 1955, 3914.
[2] Driver and Lai, *J.*, 1958, 3219.
[3] Powell, personal communication.

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TABLE 1. *Derivatives of 4,4′-dihydroxytriphenylmethane.*

Derivative	M. p.[a]	Benzene complex, m. p.[a]	Channel complex[b] M. p.	Channel complex[b] Included component (%)
3″-Nitro	162° (158·5 [1])	160° (72 [1])	ND[c]	—
2,2′-Dimethyl-3″-nitro	174 (171—172 [1])	89 (85—90 [1])	157—159°	6·4
3″-Amino	160—164 (168 [1])	110 (110 [1])	160—166	—
2″-Bromo	158 (156—157 [2])	100—120 (120 [2])	110—116	5·0
3″-Bromo-2,2′-dimethyl	218 (220—221 [2])	218 (216—218 [2])	197	8·5
4″-Bromo	125—126 (124—126 [2])	90 (98 [2])	ND	9·4
2″-Chloro[d]	166	103	134—138	10·5

[a] M. p. from the literature are given in parentheses. [b] All channel compounds formed by one triphenylmethane have the same m. p. [c] ND, complex formed but property not determined. [d] Found: Cl, 11·55. $C_{19}H_{15}ClO_2$ requires Cl, 11·4%.

branched-chain, or cyclic hydrocarbons. Complexes were also prepared by precipitation from chloroform solution by addition of the second component.

The heats of formation of some twenty complexes were calculated from vapour pressures measured in a modified dew-point apparatus.[4] The temperatures observed for the appearance and disappearance of a liquid film on a cooled ground-glass surface were within 0·5°. Dew-points for at least three different temperatures were obtained and when plotted as vapour pressure against reciprocal temperature were linear over a 30° range within the limits 15 80°. The heats of formation are given in Table 2.

TABLE 2. *Heats of formation of 4,4′-dihydroxytriphenylmethane complexes (in kcal./mole).*

Triphenylmethane	Benzene	Heptane	Octane	Decane	Oct-1-ene
2″-Bromo	8·1	7·6	8·0	9·0	6·9
3″-Bromo-2,2′-dimethyl	16·3	6·0	7·3	8·6	4·7
4″-Bromo	20·2	4·9	5·5	10·6	6·4
2″-Chloro	4·1	3·6	8·7	10·8	6·5

Isoprene complexes were formed in the same way. Polymerisation was accomplished in the presence of excess of isoprene by using γ-rays (cobalt 60) to a total dose of $1·3 \times 10^7$/r. After the complex had been washed with isopentane to remove any externally formed polymer, the included polyisoprene was isolated by dissolving the triphenylmethane in acetone. At this dose, a conversion of *ca.* 10% was obtained.

DISCUSSION

Channel complexes were not obtained when the unsolvated triphenylmethane was recrystallised in presence of the second component: the former was too insoluble. However, addition of a trace of methyl alcohol brought about complex formation within 1—2 days at room temperature. Gas chromatography of the hydrocarbon after its release from the complex did not reveal any gross contamination by methyl alcohol, the maximum amount of which was 0·02%.

Molecules which gave rise to channel complexes were the n-alkanes, n-alkenes, and the branched molecules 2,2,4-trimethylpentane, di-isobutene, and squalane. All the triphenylmethanes used, except 3″-bromo-2,2′-dimethyl-4,4′-dihydroxytriphenylmethane, gave normal channel complexes with dipentene. From the known size of dipentene, it appears that the channels within the crystals were at least 6·5 Å in diameter (with the one exception mentioned). A slight increase in the diameters of the rings in the *X*-ray powder photograph of the dipentene complex of 3″-bromo-2,2′-dimethyl-4,4′-dihydroxytriphenylmethane presumably resulted from a distortion of the crystal lattice by the included molecule, indicating that the channels are probably *ca.* 6·0 Å in diameter.

Examination of the benzene complex, the channel complexes, and the free triphenylmethane by *X*-ray powder methods showed the presence of either two or three different crystal structures associated with each triphenylmethane. Only two crystal structures arose when the triphenylmethane and the complex were isomorphous, *e.g.*, for 4,4′-dihydroxy-3″-nitro- and 3″-amino-4,4′-dihydroxy-triphenylmethane.

[4] Redlich, Gamble, Dunlop, and Millar, *J. Amer. Chem. Soc.*, 1950, **72**, 4153.

The complexes with benzene are of a different type from those with aliphatic compounds, having not only a different crystal structure but also a definite molecular composition. In the other complexes the weight ratio of the two components is constant irrespective of chain length of included component.

The benzene complexes of 4,4′-dihydroxy-2,2′-dimethyl-3″-nitro- and 3″-amino-4,4′-dihydroxy-2,2′-dimethyl-triphenylmethane were isomorphous. The channel complexes were also isomorphous although the free hosts had different crystal structures. That the channel compounds were isomorphous, and that the benzene complexes were isomorphous but that the free triphenylmethanes were not, was shown by *X*-ray powder photographs and was consistent with the infrared spectra.

2″-Chloro- and 2″-bromo-4,4′-dihydroxytriphenylmethane showed a similar tendency, as judged by the *X*-ray photographs, whereby the benzene complexes were isomorphous and the channel complexes were isomorphous although the free triphenylmethanes were not. The crystal relations were not confirmed in these two cases by infrared absorption spectroscopy but this was probably due to the very low stabilities of the complexes examined.

Some of these complexes were unstable, desolvation occurring very readily in the atmosphere. Measurement of the heats of formation (Table 2) confirmed this. The increase in heat of formation with increasing chain length shows few signs of being regular but is believed to be a genuine effect. From the accuracy of the measurements and from the reproducibility of the results, the heats of formation should be within $\pm 0{\cdot}5$ kcal./mole. The irregular increase in heat of formation with chain length would be expected if the channel is irregular, *i.e.*, where interaction (steric effects) can occur between the substituent groups of the triphenylmethane that extend into the channels and the included components. This could occur without significant change in the *X*-ray powder photographs. Such a situation is different from that of the urea complexes where the host is arranged in a helix having six molecules of urea per turn,[5] the heats of formation there increasing fairly regularly.[4]

Polymerisation of isoprene was accomplished in three complexes, *i.e.*, those with 2″-chloro-4,4′-hydroxy-, 3″-bromo-4,4′-hydroxy-2,2′-dimethyl-, and 4″-bromo-4,4′-dihydroxy-triphenylmethane. Structure determination by infrared and near-infrared spectroscopy showed that the *cis*-1,4- to *trans*-1,4-ratio was *ca.* 1 : 9, very little different from that in emulsion-polymerisation. 1,2- and 3,4-Addition was reduced almost to zero. Apart from this there were no signs of steric factors affecting the polymerisation.

Urea complexes containing aliphatic esters have been examined by infrared spectroscopy, and considerable information obtained concerning the configuration of the included molecules.[6] Unfortunately, although aliphatic esters do interact with the 4,4′-dihydroxytriphenylmethanes the complexes are of a very different kind, probably involving hydrogen bonding between the ester and the phenolic hydroxyl groups.

The formation of complexes between 4,4′-dihydroxytriphenylmethanes and long-chain hydrocarbons, the inclusion also of branched and cyclic hydrocarbons, and the formation of polymers within the lattice indicate that long channels occur in the parent crystals. That these channels are discrete is indicated by the almost complete lack of 1,2- and 3,4-addition in the isoprene polymerisation. The channels are quite large but may have regular constrictions.

The structure determinations on the polyisoprenes were carried out by P. J. Corish. We thank Mr. H. M. Powell, F.R.S., for bringing the problem to our notice and for several discussions.

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Dunlop Research Centre, Birmingham, 24. [*Received, March 31st*, 1960.]

[5] Smith, *Acta Cryst.*, 1952, **5**, 224.
[6] Barlow and Corish, *J.*, 1959, 1706.

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71. *Polynuclear Compounds. Part I. Magnetic Properties of Some Binuclear Complexes.*

By A. Earnshaw and J. Lewis.

The variation of magnetic susceptibility with temperature of a series of binuclear complexes of iron and chromium with one, two, and three bridging groups has been determined. The results have been used to determine the value of the exchange integral ($-J$) between the magnetic ions. When the bridging groups are chlorine or the hydroxyl group only a small interaction is observed. However, in the case of the basic rhodo-complexes $[(NH_3)_5Cr{\cdot}O{\cdot}Cr(NH_3)_5]Br_4$ a marked magnetic interaction has been observed and this has been associated with the possibility of π-bonding between the chromium ions and the oxygen of the bridge. A similar type of interaction has been observed in the case of a phenanthroline–iron(III) complex. Additional evidence for π-bonding involving metal and oxygen has been obtained from a study of the infrared absorption spectra of the complexes.

The study of the magnetochemistry of the transition elements has been mainly concerned with systems in which the interaction between the metal ions is considered to be negligible, *i.e.*, magnetically dilute compounds, and those in which the interaction may be considerable, *i.e.*, ferromagnetic and antiferromagnetic compounds. Polynuclear compounds are a valuable intermediate class and we are investigating the general interactions which occur in such compounds.

A binuclear compound can be considered as being formed by the combination of two mononuclear complex ions with one, two, three, or four bridging groups. If the interaction between the metal atoms is dependent on the distance between them, and no distortion is assumed to take place on formation of the complex, then the interaction will decrease in the order tetra- > tri- > di- > mono-bridged. If, however, the interaction is similar to that observed in many antiferromagnetic substances and requires the participation of the bridging group it will depend on the nature of this group and may also depend markedly on the M–L–M bond angle. We have investigated the magnetic interaction in a number of binuclear complexes of chromium and iron with a variation in the number and type of bridging groups.

Discussion

If we assume that the interaction between the two metal ions in a binuclear complex can be represented by the exchange integral, $-J$, then following the general procedure of Kambe [1] and Abragam and his co-workers [2] who calculated the susceptibilities of tri-nuclear complexes, the Hamiltonian for the system will be given by $H = -2JS_1{\cdot}S_2$ where S_1 and S_2 are the spin vectors of the two ions.

The variation of the atomic susceptibility, χ_A, with temperature for the metal will be given by the following equation [3] for the various values of $S = 5/2, 3/2, 1/2$:

$S = 5/2, 5/2$

$$\chi_A = \frac{3K}{T}\left[\frac{55 + 30\exp(10x) + 14\exp(18x) + 5\exp(24x) + \exp(28x)}{11 + 9\exp(10x) + 7\exp(18x) + 5\exp(24x) + 3\exp(28x) + \exp(30x)}\right] + N(\alpha)$$

$S = 3/2, 3/2$

$$\chi_A = \frac{K}{T}\left[\frac{42 + 15\exp(6x) + 3\exp(10x)}{7 + 5\exp(6x) + 3\exp(10x) + \exp(12x)}\right] + N(\alpha)$$

$S = 1/2, 1/2$

$$\chi_A = \frac{K}{T}\left[\frac{3}{3 + \exp(2x)}\right] + N(\alpha)$$

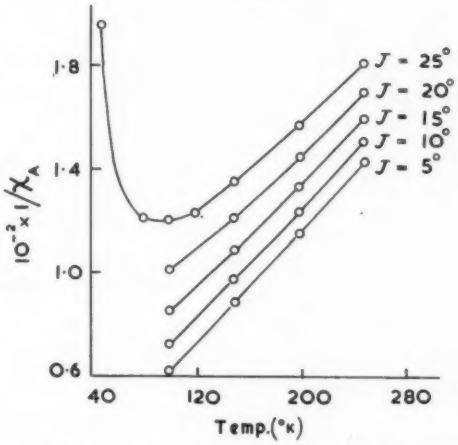
Where $K = g^2N\beta^2/3k$, $\chi = -J/kT$,

[1] Kambe, *J. Phys. Soc. Japan*, 1950, **5**, 48.
[2] Yvon, Horrowitz, and Abragam, *Rev. Mod. Phys.*, 1953, **25**, 165.
[3] Earnshaw and Lewis, *Nature*, 1958, **181**, 1262.

and g is the spectroscopic splitting factor, β is the Bohr magneton, k is Boltzmann's constant, T is the temperature, and $N(\alpha)$ is the temperature-independent paramagnetic term.

The separation between the level specified by the quantum number S^1, and the ground level is given by $J\{S^1(S^1 + 1)\}$. Thus the singlet–triplet separation in a binuclear complex would be $2J$, and the triplet–quintet separation $4J$. Often the singlet–triplet separation is defined as J (see ref. 4), so that the values of J obtained differ by a factor of 2 from those given by this theory. The curve of $1/\chi$ against T being considered for the case where $S = 3/2$, which is appropriate for spin-free, tervalent Cr (Fig. 1), the presence of an interaction J would normally be detected by a finite value of θ in the Curie–Weiss equation, *i.e.*, $\chi = C/(T + \theta)$. As the value of J increases, the deviation from a Curie plot becomes more marked and the value of θ increases. Magnetic interaction of the above type can be detected by the occurrence of an appreciable value of θ, although this type of interaction

FIG. 1.



is only one of several possible causes for a significant value of θ. It is also noticeable from these curves that a small value of the exchange integral $(-J)$ gives an appreciable value of θ, and marked magnetic deviation occurs as the temperature approaches J, with the production of a minimum in the curve.

Very few magnetic measurements have been made on polynuclear compounds. Welo [5] carried out measurements on some trinuclear complexes of chromium and iron, and these were interpreted by Kambe [1] as indicating interactions of the order of $-14°$ for chromium and $-40°$ for iron. In the case of trinuclear complexes, the situation is complicated, for two different values of J must be considered, corresponding to the interaction of the terminal atoms with the central atom and the two terminal atoms with each other. Recently, very precise data have been obtained for copper acetate and other copper salts of aliphatic carboxylic acids by Figgis and Martin [4] and Martin and Waterman; [6] the theory corresponding to $S = 1/2$ has been fully developed for these compounds. The data indicate that in these systems J is of the order of 225°, and the interaction has been considered to occur through the formation of a δ-bond between the two copper atoms in the complexes. Wilmarth, Graff, and Gustin [7] reported measurements on the binuclear chromium complexes, termed the erythro- and rhodo-salts, and observed θ values of the order of 100°, but did not attempt any theoretical interpretation of their results.

[4] Figgis and Martin, *J.*, 1956, 3837.
[5] Welo, *Phys. Rev.*, 1928, **32**, 320.
[6] Martin and Watermann, *J.*, 1957, 2545.
[7] Wilmarth, Graff, and Gustin, *J. Amer. Chem. Soc.*, 1956, **78**, 2683.

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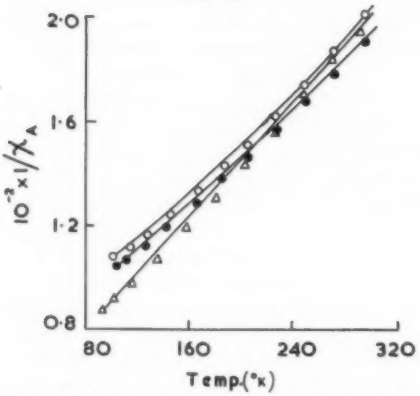
In addition to these measurements, there are the series of diamagnetic polynuclear complexes such as the metal carbonyl complexes where metal–metal bonding is considered to occur. These carbonyls correspond to polynuclear complexes in which the singlet–triplet separation is much greater than kT, with virtually complete occupation of the singlet level at room temperature. This form of magnetic behaviour would occur if the value of J was of the order of $-1000°$.

In the case of the measurements we report, the compounds can be divided into three categories depending upon the number of bridging groups involved in the complexes.

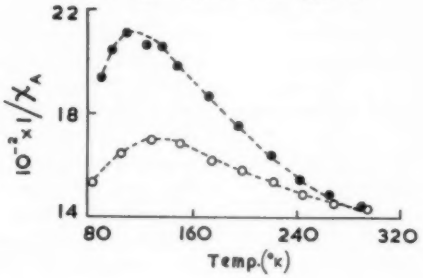
(a) *Complexes with one bridging group.* An interesting series of binuclear chromium compounds containing a single bridging group are the erythro- and rhodo-series of salts. These complexes have recently been shown by Wilmarth

FIG. 2.



○ *Acid rhodo-bromide*; ● *acid erythro-bromide*; △ *basic erythro-bromide. Lines are calculated curves.*

FIG. 3. $[(NH_3)_5Cr{\cdot}O{\cdot}Cr(NH_3)_5]Br_4$.



et al.[7] to be binuclear complexes involving hydroxy- and oxo-bridging groups, the acid erythro-series being $[(NH_3)_5Cr{\cdot}OH{\cdot}Cr(NH_3)_4(H_2O)]X_5$ and the acid rhodo-salts being $[(NH_3)_5Cr{\cdot}OH{\cdot}Cr(NH_3)_5]X_5$; the basic salts are formed by loss of a proton from the bridging hydroxyl group in the case of the rhodo-salts and from the aquo-group in the erythro-series. Thus the acid and basic erythro-salts and the acid rhodo-salts contain a hydroxyl-bridging group, whereas the basic rhodo-salt contains an oxo-bridging group.

For the acid and basic erythro- and acid rhodo-salts the plot of $1/\chi$ against T is given in Fig. 2. The compounds show the typical behaviour of binuclear complexes, with a small value of the exchange integral. Table 1 contains the values of J, g, and $N(\alpha)$ required to give the theoretical curves. In the case of a low value of J, the theoretical plot is very sensitive to the value of g used. There is a pronounced curvature of plot of $1/\chi$ against T, and the assignment of the θ can only be approximate. The value of $\mu_{eff.}$ changes from 3·5 B.M. at room temperature to a value of about 2·8 B.M. at 100° K (see Table 2). The values of g observed are those to be expected for a chromium(III) complex, where g is normally of the order of 2, since the ^4F term is split under a cubic crystal field into an orbital singlet lying lowest and two orbital triplets separated by an energy value much greater than kT.

In the case of the basic rhodo-salt, as noted by Wilmarth *et al.*[7] and Schäffer,[8] a considerable divergence from the behaviour of a mononuclear chromium salt is observed, the moment being reduced to 1·3 B.M. at room temperature. The moment, however,

[8] Schäffer, *J. Inorg. Nuclear Chem.*, 1958, **8**, 149.

falls sharply as the temperature is reduced (see Table 2). Fig. 3 gives typical results observed for this salt. The general magnetic behaviour was variable, depending upon the sample, a phenomenon also observed by Schäffer.[8] This probably arises from the

TABLE 1.

Compound	$\mu_{eff.}$ at 20° c (B.M.)	J	g	$N(\alpha) \times 10^6$	θ
Acid rhodo-bromide	3·44	−20·25°	1·94	62	120°
Acid erythro-bromide	3·52	−20·7	1·99	56	130
Acid erythro-chloride	3·62	−20·7	1·99	56	130
Basic erythro-bromide	3·50	−14	1·91	56	70
$[pyH]_5[Cl_5Fe{\cdot}Cl{\cdot}FeCl_5]$	5·57	−1·5	1·92	0	12
$[(phen)_2Cr(OH)_2Cr(phen)_2]I_4,4H_2O$	3·67	−10	1·99	58	35
$[(gly)_2Cr(OH)_2Cr(gly)_2],H_2O$	3·80	−6	2·01	52	20
$[(phal)_2Cr(OH)_2Cr(phal)_2]$	3·84	−7	2·03	44	30
$[QH]_4[Cl_4FeCl_2FeCl_4]$	5·77	−1·6	1·99	0	15
$[Et_4N]_2[Cl_2CrCl_2CrCl_2]$	3·94	−5	2·08	46	12
$[pyH]_3[Cl_3FeCl_3FeCl_3]$	6·00	−1·7	2·09	0	10

py = pyridine; phen = *o*-phenanthroline; gly = glycine; phal = phenylalanine; Q = quinoline

TABLE 2. *Experimental atomic susceptibilities (c.g.s.) and magnetic moments (B.M.) at various temperatures.*

Acid erythro-bromide

Temp. (K)	293·7°	268·4°	246·6°	224·0°	201·5°	182·6°	162·5°	139·4°	122·8°	107·3°	100·4°
$10^6\chi_A$	5230	5590	5970	6380	6845	7240	7765	8430	8920	9360	9565
$\mu_{eff.}$	3·52	3·48	3·45	3·39	3·34	3·27	3·19	3·08	2·97	2·85	2·78

Acid erythro-chloride

Temp. (K)	290·8°	269·8°	248·0°	223·9°	200·4°	174·0°	149·4°	115·5°	101·2°
$10^6\chi_A$	5510	5590	6000	6410	6960	7310	8240	9260	9660
$\mu_{eff.}$	3·60	3·49	3·46	3·40	3·36	3·20	3·15	2·94	2·81

Basic erythro-bromide

Temp. (K)	292·8°	271·1°	248·7°	227·0°	204·7°	181·8°	159·2°	136·4°	117·7°	103·3°	94·2°
$10^6\chi_A$	5174	5462	5907	6412	7017	7717	8447	9407	10,247	10,962	11,412
$\mu_{eff.}$	3·50	3·46	3·44	3·43	3·40	3·36	3·29	3·22	3·12	3·02	2·94

Acid rhodo-bromide

Temp. (K)	294·5°	268·8°	246·5°	224·5°	204·0°	185·0°	165·0°	143·4°	125·8°	112·5°	99·0°
$10^6\chi_A$	5230	5590	5970	6380	6845	7240	7765	8430	8920	9360	9565
$\mu_{eff.}$	3·44	3·41	3·38	3·35	3·31	3·24	3·17	3·07	2·94	2·85	2·73

Basic rhodo-bromide

Temp. (K)	294·7°	266·9°	244·6°	222·2°	196·6°	173·9°	150·1°	138·1°	126·3°	111·8°	99·4°
$10^6\chi_A$	702	676	652	611	572	535	503	484	484	472	488
$\sigma_{eff.}$	1·29	1·21	1·13	1·05	0·95	0·87	0·78	0·73	0·70	0·65	0·63
Temp. (K)	91·4°	295·0°	269·0°	245·0°	222·0°	198·0°	175·8°	151·0°	129·0°	106·0°	83·5°
$10^6\chi_A$	515	703	692	681	652	637	622	596	591	608	652
$\mu_{eff.}$	0·62	1·29	1·23	1·16	1·08	1·01	0·94	0·85	0·78	0·78	0·66

Pyridinium μ-chloro-bis[pentachloroferrate(III)].

Temp. (K)	295·5°	250·2°	221·4°	178·4°	144·6°	106·0°	79·5°
$10^6\chi_A$	13,070	15,260	17,240	21,050	25,720	33,710	44,450
$\mu_{eff.}$	5·58	5·55	5·55	5·50	5·48	5·37	5·34

Di-μ-hydroxy-bis[di-*o*-phenanthrolinechromium(III)] iodide tetrahydrate

Temp. (K)	292·0°	274·8°	261·1°	246·2°	232·5°	215·4°	207·2°	196·2°	178·5°	168·0°	159·4°
$10^6\chi_A$	5720	6030	6330	6690	7000	7410	7760	8090	8770	9240	9600
$\mu_{eff.}$	3·67	3·66	3·65	3·64	3·62	3·59	3·60	3·58	3·55	3·54	3·51
Temp. (K)	152·8°	143·5°	135·5°	126·0°	120·5°	109·8°	101·8°	93·5°			
$10^6\chi_A$	9940	10,400	11,000	11,600	12,190	13,000	13,700	14,810			
$\mu_{eff.}$	3·50	3·47	3·47	3·43	3·44	3·39	3·35	3·34			

Di-μ-hydroxy-bis[di(glycine)chromium(III)] monohydrate

Temp. (K)	306·3°	296·7°	274·8°	252·2°	228·2°	205·1°	188·5°	159·0°
$10^6\chi_A$	5780	6080	6440	7030	7750	8570	9290	10,750
$\mu_{eff.}$	3·78	3·81	3·78	3·78	3·78	3·77	3·76	3·71
Temp. (K)	141·0°	117·8°	98·4°	88·0°				
$10^6\chi_A$	11,960	14,000	16,080	17,310				
$\mu_{eff.}$	3·69	3·65	3·57	3·51				

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TABLE 2. (*Continued.*)

Di-μ-hydroxybis[di(phenylalanine)chromium(III)]

Temp. (K)	297·6°	285·0°	270·6°	253·3°	241·1°	224·9°	210·4°	195·4°
$10^6\chi_A$	6160	6320	6650	7060	7400	7890	8470	9020
$\mu_{eff.}$	3·85	3·81	3·81	3·80	3·79	3·78	3·79	3·77
Temp. (K)	181·6°	165·2°	150·8°	134·4°	118·6°	103·6°	89·0°	
$10^6\chi_A$	9580	10,380	11,210	12,580	13,490	15,000	17,000	
$\sigma_{eff.}$	3·75	3·72	3·69	3·69	3·59	3·54	3·34	

Quinolinium di-μ-chlorobis[tetrachloroferrate(III)]

Temp. (K)	294·6°	255·3°	207·8°	169·4°	106·0°
$10^6\chi_A$	14,030	16,250	20,000	24,030	35,370
$\mu_{eff.}$	5·78	5·78	5·79	5·73	5·50

Tetraethylammonium tri-μ-chlorobis[trichlorochromate(III)]

Temp. (K)	296·5°	281·4°	265·6°	244·5°	219·4°	196·3°	175·8°	152·6°	134·0°	115·0°	112·4°
$10^6\chi_A$	6550	6820	7200	7850	8700	9740	10,800	12,290	13,780	15,310	15,780
$\mu_{eff.}$	3·96	3·93	3·93	3·93	3·92	3·92	3·91	3·89	3·86	3·86	3·77
Temp. (K)	98·0°	88·8°	80·0°								
$10^6\chi_A$	17,620	18,950	20,290								
$\mu_{eff.}$	3·73	3·68	3·62								

Pyridinium tri-μ-chlorobis[trichloroferrate(III)]

Temp. (K)	295·8°	284·1°	261·5°	238·3°	218·7°	199·0°	180·0°	162·0°	145·0°
$10^6\chi_A$	15,130	15,580	17,150	18,760	20,550	22,690	24,420	26,900	30,180
$\mu_{eff.}$	6·01	5·98	6·01	6·00	6·02	6·03	5·96	5·93	5·94
Temp. (K)	128·5°	111·1°	99·0°	93·3°					
$10^6\chi_A$	34,100	38,410	42,770	44,520					
$\mu_{eff.}$	5·94	5·87	5·84	5·79					

Iron(III)–phenanthroline chloride complex

Temp. (K)	356·6°	346·4°	333·0°	316·5°	279·0°	253·5°	229·2°	208·8°	187·0°
$10^6\chi_A$	1427	1419	1392	1381	1381	1358	1336	1305	1259
$\mu_{eff.}$	2·03	1·99	1·93	1·88	1·76	1·67	1·57	1·48	1·38
Temp. (K)	161·8°	139·0°	117·5°	105·5°	98·3°	95·7°	90·1°		
$10^6\chi_A$	1183	1092	981	909	871	821	814		
$\mu_{eff.}$	1·25	1·11	0·96	0·88	0·83	0·80	0·77		

presence of a small concentration of the basic erythro-salt which analytically would be difficult to detect. As the temperature is lowered the susceptibility of the erythro-salt rises, and at 100° χ_A is of the order of $10{,}000 \times 10^{-6}$ c.g.s., so that the presence of a small percentage of this complex would have a marked effect on the susceptibility over the lower temperature range; the differences in susceptibility noted in Fig. 3 could arise from the presence of about 1% of the erythro-salt. We have attempted to remove this impurity by sealing samples of the basic rhodo-bromide in tubes with liquid ammonia for periods of up to two days, but the susceptibility of the sample did not change on this treatment.

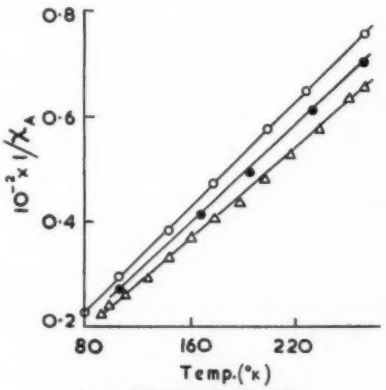
Schäffer noted a marked difference between the ultraviolet spectra of the basic rhodo-complex and the acid rhodo- and erythro-complexes, and has suggested, as also have Wilmarth *et al.*,[7] that the large reduction in magnetic behaviour may be associated with the presence of π-bonding between the chromium ions and the oxygen in the bridge. This is essentially the explanation used by Dunitz and Orgel[9] to account for the diamagnetism of the chloro-ruthenium complex $K_4[Ru_2OCl_{10}],H_2O$. In the case of the basic erythro-salt in addition to this π-bonding mechanism there must be a further interaction leading to the reduction in moment, as the direct application of Dunitz and Orgel's theory gives a moment corresponding to one unpaired electron per chromium atom. The order of energy levels in the case of the ruthenium–oxygen system was given as $[Eu^b][(B_{2g})(B_{2u})(E_g)][Eu^a]$. For the ten electrons of the chromium–oxygen system (three from each chromium atom and four from the oxygen), the non-bonding E_g orbital would be thus doubly occupied, with the resultant moment of one unpaired electron per chromium.

[9] Dunitz and Orgel, *J.*, 1953, 2594.

This behaviour is similar to that observed [10] for some binuclear oxy-bridging complexes of rhenium(IV) containing the ion $[Re_2OCl_{10}]^{4-}$. These compounds were found to be diamagnetic, whereas a moment corresponding to one unpaired electron might have been expected. In agreement with the suggested π-bonding between the oxygen and the chromium ions, we have observed the appearance of bands in the infrared absorption spectra at 854 and 870 cm.$^{-1}$. This is in the absorption range that has been found for systems containing oxygen double-bonded to metals.[11]

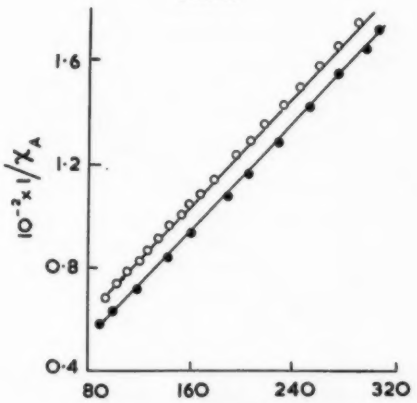
The basic rhodo-salt is thus an example of interaction occurring through an intermediate ligand group, as occurs in the super-exchange mechanism suggested to explain interaction in antiferromagnetic compounds.[12] The smaller interaction observed in the erythro- and acid rhodo-salts may be associated with a metal–oxygen–metal bond angle of the order of 120°, rather than 180° as may occur in the basic rhodo-salt. The linear system leads to a much more favourable interaction, for when the oxygen uses *sp* hybrid

FIG. 4.



○ $(pyH)_5[Cl_5Fe{\cdot}Cl{\cdot}FeCl_5]$.
● $(QH)_4[Cl_4FeCl_2FeCl_4]$.
△ $(pyH)_2[Cl_5FeCl_2FeCl_5]$.
Lines are calculated curves.

FIG. 5.



○ $[(phen)_2Cr(OH)_2Cr(phen)_2]I_4.4H_2O$.
● $[(gly)_2Cr(OH)_2Cr(gly)_2].H_2O$.
Lines are calculated curves.

bonds to form a σ-bond to the metal, the remaining *p* orbitals may form a π-bonding system with the metal d_{xy}, d_{yz}, or d_{zz} orbitals. There is, however, the possibility that, in the case of the basic rhodo-salt, the complex may contain more than two chromium atoms per molecule, as no direct molecular-weight determinations have been made owing to the insolubility of the salts. In this case the interaction may take place over a number of metal–oxygen bonds. With the acid erythro- and rhodo-salts determinations of the molecular weight from *X*-ray measurements have shown them to be binuclear complexes.

The remaining single-bridging complex investigated was the chloro-bridged iron compound $(pyH)_5[Cl_5Fe{\cdot}Cl{\cdot}FeCl_5]$, where py = pyridine. The plot of $1/\chi$ against T is given in Fig. 4, and the theoretical curve corresponded to $J = -1{\cdot}5°$, $g = 1{\cdot}92$, $N(\alpha) = 0$. The pyridine in this complex has been shown from infrared measurements, to be all present as pyridinium ion, as the characteristic absorption appearing in the 1450 cm.$^{-1}$ region which occurs when pyridine is co-ordinated to a metal ion [13] is absent in this complex.

[10] Jezowska-Trzebiatowska and Wajda, *Bull. Acad. polon. Sci.*, Cl. III, 1954, **2**, 249.
[11] Barraclough, Lewis, and Nyholm, *J.*, 1959, 3552.
[12] Lidiard, *Rep. Progr. Phys.*, 1954, **17**, 201.
[13] Sharp, personal communication.

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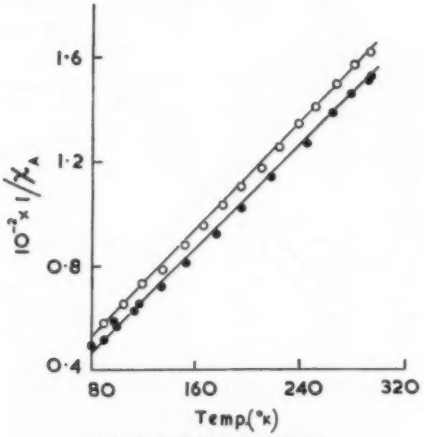
In the case of ferric complexes, the effect of a given value of $-J$ on the magnetic properties will be more marked than with chromium complexes, as the separation of the ground level, $S = 0$, to the highest level, $S = 3$ in the case of chromium and $S = 5$ in that of iron, will be $12J$ and $30J$ respectively.

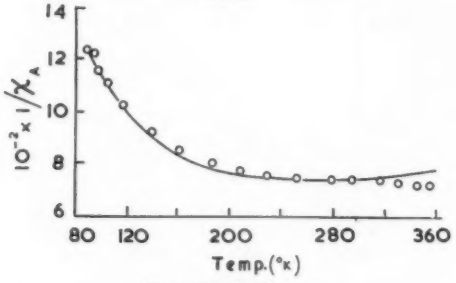
(b) *Complexes with two bridging groups.* Four compounds that definitely fall into this class have been investigated. They are the dihydroxychromium complexes with glycine, phenylalanine, and phenanthroline as the other ligands, and a di-chloro-bridged iron complex. The plots of $1/\chi$ against T (Figs. 4, 5, and 6) all suggest slight interaction in the systems, and the J, g, and $N(\alpha)$ values for the theoretical curves are given in Table 1. The susceptibilities are very little different from those of the free-ion value at room temperature, but fall below this value at lower temperatures. However, all the lines show a slight curvature which can normally only be detected by determining a sufficient number of points on the graph. The g values obtained are very close to 2, indicating the

FIG. 6.



○ $[(phal)_2Cr(OH)_2Cr(phal)_2]$.
● $(NEt_4)_2[Cl_2CrCl_2CrCl_2]$.
Lines are calculated curves.

FIG. 7. *Iron(III)–phenanthroline chloride tetrahydrate complex.*



Line is calculated curve.

absence of any appreciable orbital contribution to the moment, as would be expected for chromium(III) and spin-free iron(III) complexes.

A complex that can be considered formally to be of this class is the phenanthroline–iron compound obtained on adding phenanthroline to ferric chloride solutions. This has been given [14] the structure $[(phen)_2Fe(OH)_2Fe(phen)_2]Cl_4$. The plot of $1/\chi$ against T is given in Fig. 7, and a considerable reduction in moment occurs at low temperatures. The general characteristics of the curve can be reproduced if it is assumed that the complex is a spin-paired iron(III) compound with $J = 200°$, $N(\alpha) = 628$, and $g = 1{\cdot}97$ (full line in Fig. 7). If the compound is a binuclear complex with an oxygen bridge, as suggested for the basic rhodo-salts, then the high value of J may be accounted for on a similar π-bonding mechanism. The moment per iron atom would then correspond to one unpaired electron, the two unpaired electrons of the iron atoms occupying the anti-bonding $[Eu^a]$ orbital, so the reduction in moment below this value at lower temperatures involves a further interaction between the two electrons, as occurs with the chromium and rhenium complexes discussed above. Such a complex would involve an asymmetric ligand field,

[14] Gaines, Hammett, and Walden, *J. Amer. Chem. Soc.*, 1936, **58**, 1668.

and the T_{2g} orbital of the iron would be split into a lower singlet and upper doublet. The high value for the temperature-independent paramagnetic term may then arise from the presence of this upper doublet level. However, it is difficult to reconcile this mechanism with a g value of 1·97, as such a mechanism should lead to an aniosotropic g of average value of the order of 2·3. The problem in the case of this complex is complicated by the fact that the singlet–triplet separation is of the order of the spin–orbit coupling [Fe(III) = 440 cm.$^{-1}$], and calculations are being carried out by Dr. Figgis on this system with a simultaneous perturbation by spin–orbit coupling and exchange interaction. However, the infrared spectrum of this compound, as that of the basic rhodo-complex, shows in addition to the normal bonds observed in phenanthroline complexes, strong absorption in the region expected for metal–oxygen double bonds (852 cm.$^{-1}$). The presence of an oxygen bridge would also require the formulation of the complex as $[(phen)_2(H_2O)Fe{-}O{-}FeCl(phen)_2]Cl_2$ with the presence of at least one chloride ion in the co-ordination sphere of the metal, in the case of the anhydrous salt, in order to maintain the iron co-ordination number at 6. It is noteworthy that all attempts to prepare derivatives of the complex by replacement of the chloride with other anions have so far failed; this can be understood if the anions take part in the co-ordination sphere.

The iron complex behaves completely differently from the corresponding chromium complex, which appears from molecular-weight determinations to be the dimer $[(phen)_2Cr(OH)_2Cr(phen)_2]I_4$. As with the rhodo-complex no molecular-weight determinations have been made on the iron–phenanthroline complex, and this may be a polynuclear system containing a number of metal–oxygen bridging systems.

(c) *Complexes with three bridging groups.* The μ, μ^{I}, μ^{II}-trichloro-complexes of chromium(III) and iron(III), $[Cl_3MCl_3MCl_3]^{3-}$, have been investigated. The plots of $1/\chi$ against T are given in Figs. 4 and 5, and the values of J, g, and $N(\alpha)$ corresponding to the theoretical curves are given in Table 1. The interaction in both cases is extremely small. The X-ray structure of the cæsium salt of the chromium complex indicates that the chromium octahedra are distorted on formation of the binuclear complex in such a way that the chromium ions move apart [15]; the iron complex ion probably has a similar structure, as the cæsium salts have been shown by X-ray measurements to be isomorphous. The behaviour of the chromium compound is in sharp contrast to that of the corresponding tungsten complex ion $[W_2Cl_9]^{3-}$, where the X-ray data indicate a very short tungsten–tungsten distance.[16] In this complex the resultant diamagnetism can be explained by the formation of a direct tungsten–tungsten bond.

The results obtained for this series of compounds imply that the major interaction occurs when a bridging group such as oxygen is present, for then a π-bonding mechanism can operate between the metal–ligand–metal system. In the case of hydroxyl and chloride ions, the interaction is very much smaller, and may then occur by the delocalisation of electrons from the metal ion into anti-bonding orbitals of the bridging group. In the chromium compounds, the interaction appears to decrease with increasing multiplicity of the bridging groups, although it has not been possible to investigate a series involving the same bridging group.

Experimental

The erythro- and rhodo-compounds were prepared as described by Jörgensen [17] and by Wilmarth *et al.*[7]

The analyses of the compounds were as follows: they are best characterised by their nitrogen analyses. Acid rhodo-bromide (Found: N, 20·3; Cr, 15·2; Br, 58·0. Calc. for $H_{21}Br_5Cr_2N_{10}O$: N, 20·3; Cr, 15·05; Br, 57·85%). Basic rhodo-bromide (Found: N, 23·2; Cr, 16·9; Br, 52·6. Calc. for $H_{30}Br_4Cr_2N_{10}O$: N, 22·95; Cr, 17·05; Br, 52·4%). Acid

[15] Wessel and Ijdo, *Acta Cryst.*, 1957, **10**, 466.
[16] Watson and Waser, *Acta Cryst.*, 1958, **11**, 689.
[17] Jörgensen, *J. prakt. Chem.*, 1882, **25**, 398.

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erythro-chloride (Found: N, 26·7; Cr, 22·3; Cl, 37·9. Calc. for $H_{30}Cl_5Cr_2N_9O_2$: N, 26·8; Cr, 22·1; Cl, 37·75%). Acid erythro-bromide (Found: N, 18·8; Cr, 14·7; Br, 57·4. Calc. for $H_{30}Br_5Cr_2N_9O_2$: N, 18·25; Cr, 15·0; Br, 57·8%). Basic erythro-bromide (Found: N, 20·8; Cr, 16·7; Br, 51·9. Calc. for $H_{29}Br_4Cr_2N_9O_2$: N, 20·6; Cr, 17·0; Br, 52·3%).

Di-μ-hydroxybis[di-o-phenanthrolinechromium(III)] *iodide tetrahydrate.* This was prepared by Dwyer's method [18] (Found: C, 40·1; H, 3·1; N, 7·5%; *M*, cryoscopically in 0·7% aqueous solution, 297. Calc. for $C_{48}H_{42}Cr_2I_4N_8O_6$: C, 40·1; H, 2·9; N, 7·8%.

Di-μ-hydroxybis[di(glycine)chromium(III)] *monohydrate.* An aqueous solution (70 ml.) of chromic chloride (13·3 g.) and glycine (11·3 g.) was treated with an aqueous solution (20 ml.) of sodium hydroxide (6 g.). The pink precipitate was washed thoroughly with alcohol [19] (Found: C, 12·6; H, 4·6; N, 12·3. Calc. for $C_6H_{20}CrN_4O_{11}$: C, 21·25; H, 4·5; N, 12·4%).

Di-μ-hydroxybis[di(phenylalanine)chromium(III)]. Phenylalanine (6 g.) was refluxed with an aqueous solution (250 ml.) of tris(ethylenediamine)chromium(III) chloride (5 g.) [20] (Found: C, 54·9; H, 5·9; N, 7·3; Cr, 13·4. Calc. for $C_{36}H_{42}Cr_2N_4O_{10}$: C, 54·4; H, 5·3; N, 7·05; Cr, 13·1%).

Tristetraethylammonium tri-μ-chloro-bis[trichlorochromate(III)]. Saturated solutions of tetraethylammonium chloride (3·2 g.) and chromic chloride (1·1 g.) in methyl cyanide were mixed, and the solution was allowed to crystallise. The crystals were dried under vacuum at 100° to remove methyl cyanide [21] (Found: C, 35·5; H, 7·5; N, 7·2; Cl, 39·0; Cr, 12·8. Calc. for $C_{24}H_{60}Cl_9Cr_2N_3$: C, 35·4; H, 7·4; N, 5·2; Cl, 39·2; Cr, 12·8%).

Tripyridinium tri-μ-chlorobis[trichloroferrate(III)]. Ferric chloride (27 g.), pyridine (12 g.), and hydrochloric acid (13 ml.) were mixed, and the precipitate was recrystallised from methylated spirits [22] (Found: C, 27·2; H, 2·65; N, 6·1; Cl, 47·65; Fe, 16·4. Calc. for $C_{15}H_{18}Cl_9Fe_2N_3$: C, 26·85; H, 2·7; N, 6·3; Cl, 47·5; Fe, 16·6%).

Pentapyridinium μ-chlorobis[pentachloroferrate(III)]. Tripyridinium tri-μ-chlorobis[trichloroferrate(III)] (1 g.) was mixed with pyridine hydrochloride (2·4 g.) in alcohol (12 ml.). The compound slowly crystallised from the solution [22] (Found: C, 33·75; H, 3·4; N, 7·55. Calc. for $C_{25}H_{30}Cl_{11}Fe_2N_5$: C, 33·25; H, 3·35; N, 7·8%).

Tetraquinolinium di-μ-chlorobis[tetrachloroferrate(III)]. Quinolinium chloride (2·6 g.) was added to a solution of ferric chloride hexahydrate (2·7 g.) in concentrated hydrochloric acid (30 ml.) [22] (Found: C, 43·5; H, 3·0; N, 5·7; Cl, 35·5; Fe, 11·4. Calc. for $C_{36}H_{32}Cl_{10}Fe_2N_4$: C, 43·8; H, 3·3; N, 5·7; Cl, 35·9; Fe, 11·3%).

Iron(III)*–phenanthroline chloride tetrahydrate complex.* This substance separated from a suspension of *o*-phenanthroline in aqueous ferric chloride solution, as described by Hammett *et al.*[14] (Found: C, 53·25; H, 4·1; Fe, 10·5. Calc. for $C_{48}H_{42}Cl_4Fe_2N_8O_6$: C, 53·35; H, 3·9; Fe, 10·3%). The anhydrous compound also was analysed for iron (Found: Fe, 11·25. Calc. for $C_{48}H_{34}Cl_4Fe_2N_8O_2$: Fe, 11·1%).

We thank Dr. B. N. Figgis for many useful discussions and Dr. R. Mason for the determination of the molecular weight of the acid erythro-bromide from *X*-ray measurements.

William Ramsay and Ralph Forster Laboratories,
University College, Gower Street, London, W.C.1. [*Received, April 13th,* 1960.]

[18] Dwyer, personal communication.
[19] Ley and Ficken, *Ber.*, 1912, **45**, 377.
[20] Bailar, Stiegman, Balthis, and Huffmann, *J. Amer. Chem. Soc.*, 1939, **61**, 2402.
[21] Machin, personal communication.
[22] Weinland and Kissling, *Z. anorg. Chem.*, 1922, **120**, 209.

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72. *Some 4-Substituted Oxazoles.*

By A. B. A. Jansen and M. Szelke.

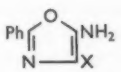
A variety of chemical transformations has been carried out on 2-phenyloxazoles bearing carboxy-, formyl-, and cyano-substituents in the 4-position. Parallel studies with 5-amino-2-phenyloxazoles bearing similar 4-substituents were less rewarding as the ring system was too readily disrupted.

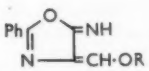
The useful properties of certain five-membered heterocyclic compounds as analgæsic, anti-inflammatory, and anti-convulsant drugs turned our attention to oxazoles, a class which has hitherto escaped detailed pharmacological examination. It was fortunate that studies related to penicillin [1] had rendered accessible several convenient starting materials.

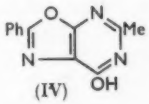
Our primary interest has been the preparation of compounds bearing a nitrogenous side chain. The ready availability of 2-phenyloxazole-4-carboxylic acid (I; X = CO_2H) from the sodium salt of 4-hydroxymethylene-2-phenyloxazolone [2] made the preparation of a series of amides (I; X = CO·NRR′) and their reduction with lithium aluminium hydride appear a simple route to amines (I; X = CH_2·NRR′). It is stated [3] that oxazoles are not stable to this reagent and that an ethoxycarbonyl group, for example, cannot be reduced to an alcohol without disruption of the ring system. We found, however, that the ester (I; X = CO_2Et) was smoothly reduced to the alcohol by the stoicheiometric quantity of lithium aluminium hydride at room temperature. With amides our success varied: amines were obtained from the diethylamide, dimethylamide, and piperidide in 24—35% yield and the reaction failed with the cyclohexylamide and di(hydroxyethyl)amide.

Another route to 4-aminomethyloxazoles proved in general to be superior. The alcohol (I; X = CH_2·OH), most conveniently prepared by reduction of the acid chloride (I; X = COCl) with sodium borohydride, was converted into its chloride by thionyl chloride and into its bromide by phosphorus pentabromide. The latter yielded the piperidide (I; X = CO·N < C_5H_{10}) in 87% yield. The reaction was also successful with morpholine and diethanolamine but failed with diethylamine. Quaternary ammonium compounds were obtained on treatment of the bromide with 1-ethylpiperidine or triethylamine.

(I)


(II)


(III)


(IV)

A few unsuccessful attempts were made to prepare 4-2′-aminoethyloxazoles (I; X = CH_2·CH_2·NRR′). The acid chloride (I; X = COCl) with diazomethane gave the crystalline diazoketone (I; X = CO·CHN_2), but efforts to effect a Wolff rearrangement were unavailing.

4-Formyl-2-phenyloxazole condensed with nitroethane under the conditions described by Shepard and his co-workers [4] to give the nitroalkene (I; X = CH:CMe·NO_2) in 47% yield, but a similar reaction with nitromethane resulted in resins. By the use of ammonium acetate instead of butylamine as the condensing agent,[5] the condensation with nitromethane occurred in 30% and that with nitroethane in 80% yield, but the products could not be reduced to the saturated amines with lithium aluminium hydride. Some intermediates for other routes to an ethylamine side chain were also prepared, *viz.*, the nitrile (I; X = CH_2·CN) (from the bromide) and the propionic acid (I; X = CH_2·CH_2·CO_2H)

[1] "The Chemistry of Penicillin," Princeton Univ. Press, 1949, Chapter 21.
[2] Cornforth and Cookson, *J.*, 1952, 1085.
[3] See Gaylord, "Reduction with Complex Metal Hydrides," Interscience Publ. Inc., New York, 1956, p. 797 for references.
[4] Shepard, Noth, Porter, and Simmons, *J. Amer. Chem. Soc.*, 1952, **74**, 4611.
[5] Cf. Young, *J.*, 1958, 3493.

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(by hydrogenation of the acrylic acid obtained by condensing the 4-aldehyde with malonic acid), but transformation of these products was not pursued.

Curtius degradation of the acid azide [2] (I; X = $CO{\cdot}N_3$) offered a route to other nitrogenous derivatives. The resulting isocyanate (I; X = $\cdot NCO$) (which was obtained crystalline, as was also its bisulphite derivative) was treated with cyclohexanol and with benzyl and 2-chloroethyl alcohol, to yield the urethanes (I; X = $NH{\cdot}CO_2C_6H_{11}$, etc.) and with allylamine, cyclohexylamine, piperidine, 3-dimethylaminopropylamine, and glycine to yield the *N*-substituted ureas (I; X = $NH{\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}CH{:}CH_2$, etc.).

We have also examined the potentiality of 5-amino-4-ethoxycarbonyl-, -4-cyano-, and -4-formyl-2-phenyloxazole (II; X = CO_2Et, CN, and CHO) which are now readily available. In general, however, the 5-amino-group greatly reduced the stability of the ring system and few of the reactions described above could be brought about with derivatives possessing this substituent.

Efforts to cause the ester (II; X = CO_2Et) to react with amines were unpromising, as mixtures resulted which could not readily be separated. With hydrazine, however, a crystalline hydrazide (II; X = $CO{\cdot}NH{\cdot}NH_2$) was obtained, which with nitrous acid gave the crystalline azide (II; X = $CO{\cdot}N_3$). Interaction of this with amines, unfortunately, gave only intractable products as did also attempts to bring about a Curtius rearrangement.

Attempts to hydrolyse the ester (II; X = CO_2Et) and its *NN*-diacetyl derivative to the amino-carboxylic acid failed, apparently as the result of disruption of the ring system. Treatment of the nitrile (II; X = CN) (prepared by the action of phosphorus oxychloride on benzamidomalondiamide) with concentrated sulphuric acid gave the crystalline amide (II; X = $CO{\cdot}NH_2$) but efforts to prepare the acid from this by hydrolysis and by treatment with nitrous acid were also unavailing.

5-Amino-4-formyl-2-phenyloxazole,[6] some of the reactions of which, for example, its red coloration with ferric chloride, suggest that it exists in the tautomeric form (III; R = H), reacted readily with benzylamine, morpholine, and piperidine, to form non-basic products which must have the open-chain structures $Ph{\cdot}CO{\cdot}NH{\cdot}C(CN){:}CHX$, where X = $NH{\cdot}CH_2Ph$, $N{<}[CH_2{\cdot}CH_2]_2{>}O$, and $N{<}C_5H_{10}$, as their infrared spectra had a strong band at 4·5 μ, characteristic of the $-CN$ group and absent from the spectrum of the aldehyde. Basic analogues were also prepared from dimethyl- and diethyl-aminoethylamine and 3-dimethylaminopropylamine. An attempt to re-form the ring system by treatment of the products with acetic anhydride led only to 4-acetoxymethylene-5-imino-2-phenyloxazoline (III; R = Ac), identified by its infrared spectrum and failure to give a colour with ferric chloride.

The oxazolopyrimidine (IV) was obtained by treating 5-acetamido-4-cyano-2-phenyloxazole with alkali and hydrogen peroxide,[7] the structural assignment being based on the analysis, solubility in alkali, and ultraviolet and infrared spectra.

Experimental

Ultraviolet spectra were measured for EtOH solutions unless otherwise stated.

2-Phenyloxazole-4-carboxyamides: *General Method.*—2-Phenyloxazole-4-carbonyl chloride (0·80 g., 0·0038 mole) in dry benzene (15 ml.) was added dropwise to a chilled solution of the amine (0·015 mole) in benzene (15 ml.). The mixture, sometimes containing precipitated amine hydrochloride, was washed successively with water, dilute hydrochloric acid, and water. After evaporation under diminished pressure the residue was crystallised from an appropriate solvent (see Table).

4-Hydroxymethyl-2-phenyloxazole.—(*a*) An ethereal M-solution (0·5 ml.) of lithium aluminium hydride was added to 4-ethoxycarbonyl-2-phenyloxazole (0·2 g.) in dry ether (10 ml.) After 10 min. at room temperature the mixture was treated with water, followed by hydrochloric

[6] Ref. 1, p. 728.
[7] Cf. Bogart and Hand, *J. Amer. Chem. Soc.*, 1902, **24**, 1031; Robins, *J. Org. Chem.*, 1958, **23**, 191.

acid. Evaporation of the water-washed ethereal layer left the oily *alcohol* which crystallised from light petroleum in needles (0·1 g.), m. p. 82—83°, $\lambda_{max.}$ 268 (ε 11,600) and 218 mμ (ε 2880) (Found: C, 68·5; H, 5·2; N, 8·1. $C_{10}H_9NO_2$ requires C, 68·55; H, 5·2; N, 8·0%).

(*b*) Sodium borohydride (0·66 g., 0·0175 mole) was added to a solution of 2-phenyloxazole-4-carbonyl chloride (0·52 g., 0·0025 mole) in dry dioxan (10 ml.) and the ensuing exothermic reaction was completed by heating the heterogeneous mixture on a steam-bath for 2 hr. The

2-Phenyloxazole-4-carboxyamides.

Amine	M. p.	Yield (%)	Found (%) C	H	N	Formula	Required (%) C	H	N
Allylamine	92—93°	81 [1]	68·4	5·3	12·15	$C_{12}H_{12}N_2O_2$	68·4	5·3	12·3
Benzylamine	146·5—148·5	94 [2]	73·45	5·3	9·75	$C_{17}H_{14}N_2O_2$	73·4	5·1	10·1
Cyclohexylamine	130—131	90 [2]	—	—	9·85	$C_{16}H_{18}N_2O_2$	—	—	10·3
Diethanolamine	97—99	26 [3] *	61·3	5·8	10·0	$C_{14}H_{16}N_2O_4$	60·85	5·8	10·1
Diethylamine	42—43	61 [3]	69·1	6·6	11·35	$C_{14}H_{16}N_2O_2$	68·8	6·6	11·15
3-Dimethylamino-propylamine hydrochloride	46—48 (b. p. 80—84/0·5 mm.) 141—142	59 [4]	58·2	6·5	12·9	$C_{15}H_{19}N_3O_2$,HCl	58·15	6·5	13·6
2-Hydroxyethyl-amine	133·5—134	88 [3]	61·9	5·3	11·55	$C_{12}H_{12}N_2O_3$	62·1	5·2	12·1
D-Glucosamine	201—202	31 [5] *	—	—	8·4	$C_{16}H_{18}N_2O_7$	—	—	8·0
Glycine	219—221	65 [1] *	59·0	4·0	12·4	$C_{13}H_{10}N_2O_4$	58·5	4·0	11·9
Guanidine	226·5—228	72 [6] *	—	—	24·0	$C_{11}H_{10}N_4O_2$	—	—	24·3
Morpholine	70·5—71·5	76 [1]	65·1	5·7	10·3	$C_{14}H_{14}N_2O_3$	65·1	5·5	10·85
Piperidine	64—66	90 [7]	70·2	6·2	10·8	$C_{15}H_{16}N_2O_2$	70·3	6·3	10·9

Solvent for crystallisation: 1, aq. EtOH; 2, aq. MeOH; 3, C_6H_6; 4, EtOH–Et_2O–HCl; 5, EtOAc; 6, $CHCl_3$; 7, EtOH; 8, Et_2O.

* A solution of the acid chloride in dioxan was added to the base in aqueous alkali in the Schotten–Baumann manner.

solvent was removed *in vacuo* and the residue dissolved in water (25 ml.). After decomposition of the unchanged sodium borohydride the mixture was extracted with ether (5 × 20 ml.). The extracts were washed, dried, and evaporated, leaving crystals (0·3 g., 68%), m. p. 80—82°. Recrystallisation from light petroleum raised the m. p. to 82—83°, not depressed on admixture with the product from (*a*).

The *acetyl derivative*, prepared with acetyl chloride in pyridine had m. p. 39·5—40° (Found: C, 66·1; H, 5·2; N, 6·15. $C_{12}H_{11}NO_3$ requires C, 66·35; H, 5·1; N, 6·45%).

4-Diethylaminomethyl-2-phenyloxazole.—A solution of 4-diethylaminocarbonyl-2-phenyloxazole (1·88 g.) in dry ether (20 ml.) was added slowly to stirred ethereal 0·9M-lithium aluminium hydride (4·8 ml.) diluted with dry ether (20 ml.). The resulting yellow liquid was stirred for 1 hr. at room temperature, then the excess of the reducing agent was decomposed with water (5 ml.), and the ethereal solution was extracted with 2N-hydrochloric acid. The combined acidic extracts were rendered strongly alkaline with 10% sodium hydroxide solution and extracted with ether. After the removal of the solvent the base was left as a yellow oil (0·75 g., 41%). The hygroscopic *hydrochloride* (0·57 g., 28%), precipitated from benzene solution by ethereal hydrochloric acid, had m. p. 138·5—140°, $\lambda_{max.}$ 262 mμ (ε 16,500) (Found: C, 62·0; H, 7·2; Cl, 13·2. $C_{14}H_{19}ClN_2O$ requires C, 63·0; H, 7·2; Cl, 13·3%). The *picrate* separated from an ethanol solution of the base and recrystallised from 90% ethanol as yellow needles, m. p. 116—116·5° (Found: C, 52·5; H, 4·7; N, 14·9. $C_{20}H_{21}N_5O_8$ requires C, 52·3; H, 4·6; N, 15·25%). The two following compounds were prepared similarly.

4-Dimethylaminomethyl-2-phenyloxazole.—The free amine was obtained as a pale yellow oil (29%). The very hygroscopic hydrochloride softens from 121°, m. p. at 154—156°, $\lambda_{max.}$ 263 mμ (ε 17,200). The *picrate* crystallised from 60% ethanol as needles, m. p. 156—158° (Found: C, 49·8; H, 4·1; N, 15·8. $C_{18}H_{17}N_5O_8$ requires C, 50·1; H, 4·0; N, 16·2%).

4-Piperidinomethyl-2-phenyloxazole.—(*a*) The free base, a pale yellow oil (35%), was converted into the *hydrochloride* (33%), m. p. 210—211°, $\lambda_{max.}$ 263 mμ (ε 17,900) (Found: C, 64·8; H, 6·9; N, 9·7. $C_{15}H_{19}ClN_2O$ requires C, 64·6; H, 6·9; N, 10·05%). The *picrate* crystallised from ethanol as needles, m. p. 186—187° (Found: C, 52·7; H, 4·6; N, 14·7. $C_{21}H_{21}N_5O_8$ requires C, 53·5; H, 4·5; N, 14·9%).

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(*b*) 4-Bromomethyl-2-phenyloxazole (see below) (0·90 g., 0·0038 mole) and piperidine (0·65 g., 0·0076 mole) were refluxed in ethanol (10 ml.) for 2 hr. After the removal of the solvent, the residual oil was taken up in water and extracted with ether. The ethereal solution was shaken with 5% hydrochloric acid, and the acidic extract was treated with sodium nitrite (0·2 g.) at 60° and extracted with ether. The aqueous solution was basified and the product collected in ether. Evaporation of the solvent from the dried (Na_2SO_4) solution left the base (0·81 g., 87%) as a colourless oil. It was converted into the hydrochloride in dry benzene with ethereal hydrochloric acid, to give needles (0·82 g., 78%), m. p. and mixed m. p. 209—210·5°.

4-Chloromethyl-2-phenyloxazole.—4-Hydroxymethyl-2-phenyloxazole (0·88 g., 0·005 mole) was treated with thionyl chloride (5 ml.), first in the cold and then under reflux for 1 hr. The excess of reagent was removed *in vacuo* and the residue, after treatment in ethanol with charcoal, was distilled. The main fraction, b. p. 158—160°/13 mm., solidified (0·68 g., 71%). Recrystallisation of this *chloride* from a very small quantity of cold (−50°) light petroleum (b. p. 80—100°) afforded needles, m. p. 55·5—56°, $\lambda_{max.}$ 266 and 216·5 mμ (ε 13,300 and 2100 respectively), (Found: C, 62·1; H, 4·05; N, 7·4. $C_{10}H_8ClNO$ requires C, 62·0; H, 4·2; N, 7·2%).

4-Bromomethyl-2-phenyloxazole.—To a solution of 4-hydroxymethyl-2-phenyloxazole (0·94 g.) in dry benzene (20 ml.) was added, with stirring, a solution of phosphorus pentabromide (2·52 g.) in dry benzene (50 ml.). The solvent was removed, leaving a yellow solid. Crushed ice was added and the crude *bromide* (1·05 g., 82%) collected. It crystallised from aqueous methanol as colourless needles, m. p. 69·5—71·5°, $\lambda_{max.}$ 268 and 210 mμ (ε 15,900 and 13,150 respectively) (Found: N, 6·1; Br, 33·8. $C_{10}H_8BrNO$ requires N, 5·9; Br, 33·8%).

4-Morpholinomethyl-2-phenyloxazole.—4-Bromomethyl-2-phenyloxazole (1·20 g., 0·005 mole) reacted with morpholine (0·88 g., 0·01 mole) at room temperature with evolution of heat. The resulting yellow syrup was extracted with benzene and the extracts were shaken with 5% hydrochloric acid. To remove any morpholine present, the acidic solution was treated with sodium nitrite (0·30 g.) at 60° and extracted with ether. The amine was precipitated by an excess of 10% sodium hydroxide solution and extracted with ether. Evaporation of the solvent left the base as a pale yellow oil (0·83 g., 68%). The *hydrochloride*, prepared in dry benzene, gave plates, m. p. 218—219·5°, $\lambda_{max.}$ 262 mμ (ε 15,700) (Found: C, 59·6; H, 6·0; Cl, 12·85; N, 10·15. $C_{14}H_{17}ClN_2O_2$ requires C, 59·9; H, 6·1; Cl, 12·6; N, 10·0%). The *picrate* crystallised from ethanol as yellow needles, m. p. 199—201° (Found: N, 14·3. $C_{20}H_{19}N_5O_9$ requires N, 14·8%).

4-Di-(2-hydroxyethyl)aminomethyl-2-phenyloxazole.—The bromide (1·20 g., 0·005 mole) and diethanolamine (0·50 g., 0·0047 mole) were refluxed in 95% ethanol (15 ml.) for 2 hr. After evaporation of the solvent, the residue was taken up in water (15 ml.) and extracted with ether. The aqueous phase was basified with 10% sodium hydroxide solution and extracted with ether. The amine was obtained as a colourless oil (0·20 g., 15%) after the removal of the solvent. The *picrate*, recrystallised twice from ethyl acetate, was obtained in yellow columns, m. p. 122·5—123·5° (Found: C, 49·0; H, 4·55; N, 14·75. $C_{20}H_{21}N_5O_{10}$ requires C, 48·9; H, 4·3; N, 14·25%).

1-Ethyl-1-(2-phenyloxazol-4-ylmethyl)piperidinium Bromide.—The bromide (1·20 g.) was heated on a steam-bath with 1-ethylpiperidine (1·13 g.) for 10 min. The resulting glass was taken up in water (15 ml.), some undissolved white solid removed, and the filtrate evaporated to dryness *in vacuo*. The residue crystallised in a desiccator over phosphorus pentoxide to give a pale yellow solid *bromide* (0·65 g., 37%), m. p. indefinite (70—100°) (Found: C, 58·5; H, 6·45; N, 7·9. $C_{17}H_{23}BrN_2O$ requires C, 58·1; H, 6·6; N, 8·0%).

NNN-Triethyl-N-(2-phenyloxazol-4-ylmethyl)ammonium Bromide.—This *compound*, prepared (78%) in an analogous manner, had an indefinite m. p. (162—173°), $\lambda_{max.}$ 261 mμ (ε 15,750) (Found: C, 55·9; H, 6·5; N, 7·8. $C_{16}H_{25}BrN_2O$ requires C, 56·6; H, 6·8; N, 8·3%).

Diazomethyl 2-Phenyloxazol-4-yl Ketone.—2-Phenyloxazole-4-carbonyl chloride (1·25 g.) in dry ether (75 ml.) was added dropwise to a stirred solution of diazomethane (0·81 g.) in ether (60 ml.). After a further 30 minutes' stirring, the solvent was removed *in vacuo*, leaving a yellow solid (1·25 g.). This *diazo-ketone* was purified by precipitation with light petroleum (b. p. 60—80°) from ether, to give yellow plates, m. p. 148—149° (decomp.), $\lambda_{max.}$ 292, 268, and 212 mμ (ε 19,200, 20,500, and 11,700 respectively) (Found: C, 61·2; H, 3·4; N, 20·1. $C_{11}H_7N_3O_2$ requires C, 61·0; H, 3·3; N, 19·7%).

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4-(2-*Nitroprop*-1-*enyl*)-2-*phenyloxazole*.—(*a*) A mixture of 4-formyl-2-phenyloxazole [8] (0·81 g., 0·005 mole), nitroethane (0·38 g., 0·005 mole), and butylamine (0·05 ml.) was left at room temperature for 10 days. A crystalline *product* was formed which, recrystallised from ethanol in yellow prisms (0·50 g., 47%), had m. p. 173—174°, $\lambda_{max.}$ 322, 272, and 209 mμ (ε 12,590, 12,720, and 13,900 respectively) (Found: C, 62·4; H, 4·3; N, 12·1. $C_{12}H_{10}N_2O_3$ requires C, 62·6; H, 4·4; N, 12·2%).

(*b*) The aldehyde (1·5 g., 0·0086 mole) and ammonium acetate (0·3 g.) were refluxed in nitroethane (10 ml.) for 35 min. On cooling, yellow columns separated (1·57 g., 79·5%) that had m. p. and mixed m. p. 172—173°.

4-2′-*Nitrovinyl*-2-*phenyloxazole*.—The aldehyde (1·5 g.) and ammonium acetate (0·3 g.) were refluxed in nitromethane (10 ml.) for 30 min. Brown crystals (0·56 g., 30%) of the *nitroalkene* separated on cooling. Recrystallisation first from aqueous ethanol, then from nitromethane, afforded yellow needles, m. p. 156—158°, $\lambda_{max.}$ 317 and 258 mμ (ε 16,200 and 14,200 respectively) (Found: C, 61·3; H, 3·9; N, 13·3. $C_{11}H_8N_2O_3$ requires C, 61·1; H, 3·7; N, 13·0%).

4-*Cyanomethyl*-2-*phenyloxazole*.—4-Bromomethyl-2-phenyloxazole, (1·2 g.) and potassium cyanide (0·50 g.) were refluxed in dry methanol (10 ml.). After 6 hr., the precipitated potassium bromide (0·65 g.) was filtered off. The dark brown filtrate was treated with charcoal and evaporated to *ca.* 5 ml. Water (3 ml.) was added and the precipitated needles (0·47 g.), m. p. 72—84°, were collected, and chromatographed in benzene (3 ml.) on deactivated alumina (200 g.). Elution with 1 : 20 chloroform–benzene afforded pale yellow crystals (0·39 g., 42%). Recrystallisation from aqueous methanol gave the *nitrile* as needles, m. p. 87·5—88·5°, $\lambda_{max.}$ 264·5 mμ (ε 14,000), (in Nujol) 4·42 μ (CN) (Found: C, 71·9; H, 4·45; N, 14·95. $C_{11}H_8N_2O$ requires C, 71·7; H, 4·4; N, 15·2%).

β-2-*Phenyloxazol*-4-*ylacrylic Acid*.—4-Formyl-2-phenyloxazole (0·5 g.), malonic acid (0·3 g.), and dry pyridine (5 ml.) were heated under anhydrous conditions on a steam-bath for 2½ hr. After cooling, the mixture was poured into dilute hydrochloric acid and the white *acrylic acid* collected. Recrystallisation from aqueous ethanol gave needles (0·37 g., 60%), m. p. 191—193·5°, $\lambda_{max.}$ 286 and 216 mμ (ε 22,600 and 20,000 respectively) (Found: N, 6·6. $C_{12}H_9NO_3$ requires N, 6·5%).

β-2-*Phenyloxazol*-4-*ylpropionic Acid*.—The acrylic acid (2·25 g.) was hydrogenated in ethanol (70 ml.) with 10% palladium–charcoal at room temperature and pressure until gas absorption ceased. After removal of the catalyst the filtrate was evaporated; the residual *propionic acid* recrystallised from ethanol as flakes (1·3 g., 58%), m. p. 86—87°, $\lambda_{max.}$ 270 mμ (ε 16,120) (Found: N, 6·4. $C_{12}H_{11}NO_3$ requires N, 6·5%).

2-*Phenyloxazol*-4-*yl Isocyanate*.—2-Phenyloxazole-4-carbonyl azide (4·1 g., 0·019 mole) was boiled in dry xylene (40 ml.) for 15 min. The solvent was removed *in vacuo* and the residue distilled to give a colourless *isocyanate* (1·9 g.), b. p. 116°/0·8 mm., m. p. sinters at 186°, m. p. 194°, $\lambda_{max.}$ 277 mμ (ε 8500) (Found: C, 64·4; H, 3·4; N, 14·8. $C_{10}H_6N_2O_2$ requires C, 64·5; H, 3·25; N, 15·05%). The product became brown in air.

The *bisulphite adduct* was prepared by shaking the isocyanate (0·83 g.) in xylene (12 ml.) with a saturated solution of sodium hydrogen sulphite (20 ml.) for 3 hr. After 20 hr. in the cold the yellow precipitate was collected and dried (0·85 g.). Washing with dioxan (20 ml.) removed some oil, leaving a white solid (0·63 g.), m. p. 173·5—174° (decomp.) $\lambda_{max.}$ 298 and 228 mμ (ε 12,660 and 17,800 respectively) (Found: C, 41·65; H, 2·85; N, 9·9. $C_{10}H_7N_2NaO_5S$ requires C, 41·25; H, 2·4; N, 9·65%).

Cyclohexyl **2-*Phenyloxazol*-4-*ylcarbamate*.**—The azide (1·07 g.) was heated in dry xylene (15 ml.) in the presence of cyclohexanol (1 ml.) until gas evolution ceased, and then for a further 3 hr. The solvent was removed at reduced pressure; the residual *carbamate* crystallised from methanol as pale yellow prisms (0·74 g., 52%), m. p. 87—88°, $\lambda_{max.}$ 290 and 221 mμ (ε 7100 and 11,000 respectively) (Found: C, 66·7; H, 6·0; N, 9·15. $C_{16}H_{18}N_2O_3$ requires C, 67·1; H, 6·3; N, 9·8%).

Benzyl **2-*Phenyloxazol*-4-*ylcarbamate*.**—This *compound* was prepared in an analogous manner. Fawn crystals (65%) obtained from methanol had m. p. 130·5—131·5°, $\lambda_{max.}$ 290 and 220 mμ (ε 8210 and 13,600 respectively) (Found: C, 69·0; H, 4·4; N, 9·8. $C_{17}H_{14}N_2O_3$ requires C, 69·4; H, 4·8; N, 9·5%).

2-Chloroethyl **2-*Phenyloxazol*-4-*ylcarbamate*** —To a solution of the isocyanate (0·83 g.) in

[8] Cornforth, Fawaz, Goldsworthy, and Robinson, *J.*, 1949, 1552.

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xylene (12 ml.) was added 2-chloroethanol (2 ml.). The *product* separated overnight (0·85 g., 63%). It crystallised from ethanol as prisms, m. p. 154·5—155·5°, $\lambda_{max.}$ 298·5 and 215·5 mμ (ε 12,100 and 16,050 respectively) (Found: C, 54·3; H, 4·2; N, 9·8. $C_{12}H_{11}ClN_2O_2$ requires C, 54·0; H, 4·1; N, 10·05%).

N-Allyl-N'-2-phenyloxazol-4-ylurea.—The azide (1·07 g., 0·005 mole) was rearranged to the isocyanate by heating it in dry xylene (15 ml.), and the cooled solution was added to allylamine (1·5 ml.) in xylene (10 ml.). Heat was evolved and the *urea* (0·75 g.), m. p. 140—142°, separated on cooling. Recrystallisation from aqueous ethanol gave prisms (0·71 g., 58%), m. p. 143—143·5°, $\lambda_{max.}$ 289 and 220·3 mμ (ε 14,600 and 25,650 respectively) (Found: C, 64·6; H, 5·3. $C_{13}H_{13}N_3O_2$ requires C, 64·2; H, 5·4%).

The following *NN'*-disubstituted ureas were prepared in a similar manner:

N-Cyclohexyl-N'-2-phenyloxazol-4-ylurea crystallised from the reaction mixture on cooling. Recrystallisation from aqueous ethanol afforded prisms (62%), m. p. 175—175·5°, $\lambda_{max.}$ 299 and 221 mμ (ε 9860 and 17,050 respectively) (Found: C, 66·9; H, 6·2; N, 14·7. $C_{16}H_{19}N_3O_2$ requires C, 67·3; H, 6·7; N, 14·7%).

1-(N-2-Phenyloxazol-4-ylcarbamoyl)piperidine recrystallised from aqueous methanol as prisms (57%), m. p. 119·5—122°, $\lambda_{max.}$ 294 and 222 mμ (ε 11,400 and 18,000 respectively) (Found: N, 15·3. $C_{15}H_{17}N_3O_2$ requires N, 15·5%).

N-3-Dimethylaminopropyl-N'-(2-phenyloxazol-4-yl)urea (47%) crystallised from benzene–cyclohexane (1 : 3) as colourless prisms, m. p. 132·5—134°, $\lambda_{max.}$ 298 and 218·5 mμ (ε 9530 and 18,250 respectively) (Found: C, 62·8; H, 6·9; N, 19·35. $C_{15}H_{20}N_4O_2$ requires C, 62·5; H, 7·0; N, 19·4%).

N-(2-Phenyloxazol-4-ylcarbamoyl)glycine.—A solution of 2-phenyloxazol-4-yl isocyanate (0·80 g., 0·0043 mole) in dry dioxan (15 ml.) was added with stirring to a solution of the sodium salt (0·41 g.) of glycine in dioxan (15 ml.) and water (8 ml.). A white solid was precipitated. A further quantity (30 ml.) of dioxan was added and the *sodium salt* (1·02 g., 79%) of the product was collected. Recrystallisation from water gave plates, sintering at 110°, m. p. 220—221° (decomp.), $\lambda_{max.}$ 299 and 221 mμ (ε 10,800 and 19,350 respectively) (Found: loss on drying, 6·1; N, 13·05. $C_{13}H_{16}N_3NaO_4,H_2O$ requires H_2O, 6·0; N, 12·95%). The free *acid* crystallised from aqueous ethanol as needles, m. p. 194·5—196° (decomp.), $\lambda_{max.}$ 296 and 219 mμ (ε 10,700 and 17,750 respectively) (Found: N, 14·85. $C_{12}H_{11}N_3O_4,H_2O$ requires N, 15·05%).

5-Amino-4-hydrazinocarbonyl-2-phenyloxazole.—A mixture of 5-amino-4-ethoxycarbonyl-2-phenyloxazole [9] (0·23 g.), hydrazine hydrate (1 ml.), and ethanol (1 ml.) was heated on a steam-bath for ¾ hr., then evaporated to dryness on the bath under reduced pressure. Water was added to the residue and the whole was again evaporated to dryness *in vacuo*. This process was repeated several times to remove all the excess of hydrazine. Finally more water was added and the insoluble material (0·15 g.), decomp. *ca.* 220°, was collected. For analysis, the *hydrazide* was recrystallised from boiling water and a little alcohol, affording prisms, decomp. 230—240°, $\lambda_{max.}$ 229·5 mμ (ε 21,480) (Found: N, 25·5. $C_{10}H_{10}N_4O_2$ requires N, 25·65%).

5-Amino-2-phenyloxazole-4-carbonyl Azide.—The 4-ethoxycarbonyloxazole (0·5 g.), hydrazine hydrate (2·25 ml.), and ethanol (5 ml.) were refluxed for ¾ hr. and then evaporated to dryness *in vacuo*. Water was added and the evaporation was repeated as in the preceding experiment. The residue was dissolved in an excess of 2N-hydrochloric acid (10 ml. more than was required for neutrality), and sodium nitrite (1·2 g.) in water (12 ml.) was added with ice-cooling until an excess was detected. The orange *azide* (0·35 g.) was collected, washed with water, and dried in a vacuum-desiccator. It was washed with a little methanol and then recrystallised from methanol, giving orange prisms (30 mg.), decomp. *ca.* 95° (Kofler), $\lambda_{max.}$ 277 mμ (ε 1095), $\lambda_{max.}$ (in $CHBr_3$) 4·67 (N_3) and 5·89 μ (CO) (Found: C, 52·3; H, 3·0. $C_{10}H_7N_5O_2$ requires C, 52·4; H, 3·1%).

5-Amino-4-carbamoyl-2-phenyloxazole.—5-Amino-4-cyano-2-phenyloxazole (3 g.) was added portionwise to concentrated sulphuric acid (8·1 ml.) with cooling at 0°. The mixture was heated for ¾ hr. on a steam-bath, and the red liquid poured into ice and water. The brown solid *amide* was collected, shaken with 2N-sodium carbonate, and recrystallised from methanol, yielding pale brown crystals (2·2 g., 66%), m. p. 172—174°, $\lambda_{max.}$ 312, 271, and 224 mμ (ε 15,400, 10,680, and 6660 respectively) (Found: C, 59·45; H, 4·6; N, 20·65. $C_{14}H_{15}N_3O_3$ requires C, 59·1; H, 4·5; N, 20·7%).

[9] Ref. 1, p. 726.

Morpholinomethylenehippuronitrile.—5-Amino-4-formyl-2-phenyloxazole (7 g.), morpholine (3·5 g.), and ethyl acetate (150 ml.) were heated on a steam-bath for 30 min. and the solution was concentrated to about 50 ml.; brown crystals of the *nitrile* separated. Recrystallisation from ethyl acetate yielded colourless needles (4·2 g., 44%), m. p. 205°, $\lambda_{max.}$ 263·5 and 227 mμ (ε 17,400 and 12,600 respectively) (Found: C, 65·2; H, 5·7; N, 16·55. $C_{14}H_{15}O_2N_3$ requires C, 65·35; H, 5·9; N, 16·3%).

Piperidinomethylenehippuronitrile.—The aldehyde (0·1 g.), piperidine (0·05 g.), and ethanol (10 ml.) were heated on a steam-bath for 30 min. and the solution was evaporated to dryness under reduced pressure. The solid *product* was recrystallised twice from ethyl acetate, yielding needles (0·01 g.), m. p. 183—184°, $\lambda_{max.}$ (in Nujol) 2·98 (NH) and 4·54 μ (CN) (Found: C, 71·1; H, 6·9. $C_{15}H_{17}N_3O$ requires C, 70·85; H, 6·4%).

2-*Dimethylaminoethylaminomethylenehippuronitrile.*—The aldehyde (1·29 g.), *NN*-dimethylethylenediamine (0·76 g.) and ethanol (50 ml.) gave, as above, a *nitrile* that crystallised from ethyl acetate as pale yellow prisms (1·4 g., 79%), m. p. 136—137°, $\lambda_{max.}$ 259·5 and 225·5 mμ (ε 12,850 and 9890 respectively) (Found: C, 64·35; H, 6·8; N, 21·3. $C_{14}H_{18}N_4O$ requires C, 65·0; H, 7·0; N, 21·7%).

2-*Diethylaminoethylaminomethylenehippuronitrile.*—The aldehyde (3 g.), *NN*-diethylethylenediamine (2 g.), and ethanol (50 ml.) yielded, as above, a gummy nitrile that was converted into the *dihydrochloride* with alcoholic hydrochloric acid. This recrystallised from ethanol–ethyl acetate as pink prisms (1·3 g., 49%), m. p. 182—183° (Found: N, 15·5; Cl, 21·1. $C_{16}H_{24}Cl_2N_4O$ requires N, 15·7; Cl, 20·7%).

3-*Dimethylaminopropylaminomethylenehippuronitrile.*—The aldehyde (4 g.), *NN*-dimethylpropylenediamine (2·8 ml.), and absolute alcohol (100 ml.) gave, as above, the *nitrile* as pale brown prisms (4·5 g., 78%), m. p. 125° (from benzene), $\lambda_{max.}$ 260 and 225 mμ (ε 18,100 and 13,000 respectively) (Found: C, 66·2; H, 7·4; N, 20·3. $C_{15}H_{20}N_4O$ requires C, 66·15; H, 7·4; N, 20·6%).

4-*Acetoxymethylene*-5-*imino*-2-*phenyloxazoline.*—Morpholinomethylenehippuronitrile (0·3 g.), acetic anhydride (5 ml.), and four drops of concentrated sulphuric acid were heated for 30 sec. on a steam-bath. The red solution was poured into water (150 ml.) and after 1 hr. the crystalline *imine* was collected and recrystallised from 95% ethanol, giving pink needles (0·13 g.), m. p. 152—153°, $\lambda_{max.}$ 285 mμ (ε 27,800), $\lambda_{max.}$ (in Nujol) 3·12, 3·27 (NH), 5·75 (Ac), and 6·16, 6·3 μ (C=N) (Found: C, 62·6; H, 4·4; N, 12·05. $C_{13}H_{10}N_2O_3$ requires C, 62·6; H, 4·4; N, 12·2%).

A similar procedure carried out with 3-dimethylaminopropylaminohippuronitrile yielded the same oxazoline.

7-*Hydroxy*-5-*methyl*-2-*phenyloxazolo*[5,4-d]*pyrimidine.*—5-Acetamido-4-cyano-2-phenyloxazole [10] (0·84 g.) was heated on a steam-bath for 2 hr. in a mixture of 10% potassium hydroxide solution (5·2 ml.) and 6% hydrogen peroxide (6 ml.), and the hot solution was treated with charcoal (0·2 g.). On cooling, crystals separated, recrystallisation of which from chloroform yielded colourless prisms (0·10 g., 12%), m. p. 314—316°, $\lambda_{max.}$ 305, 296, 223·5, and 217·5 mμ (ε 20,200, 20,200, 10,700, and 11,450 respectively), $\lambda_{max.}$ (in Nujol) 3·22, 3·29 (OH or NH), 5·8 (CO), 6·36 μ (C=N). The *compound* was soluble in aqueous alkali and precipitated unchanged on acidification (Found: C, 63·65; H, 3·9; N, 18·6. $C_{12}H_9N_3O_2$ requires C, 63·4; H, 4·0; N, 18·5%).

We are indebted to Mr. E. G. Cummins for interpretation of the infrared spectra and to Messrs. B. Gale and T. J. Russell and Miss B. Gregory for experimental assistance.

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[10] Ref. 1, p. 729.

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73. *Mechanisms of Reactions in the Sugar Series. Part III.* The Acid-catalysed Hydrolysis of t-Butyl β-D-Glucopyranoside and Other Glycosides.*

By C. Armour, C. A. Bunton, S. Patai, L. H. Selman, and C. A. Vernon.

The acid-catalysed hydrolyses of *o*-hydroxymethylphenyl β-D-glucopyranoside, lactose, maltose, and methyl 2-deoxy-α- and -β-D-glucopyranoside have been investigated. In the cases studied, bond fission occurs between the pyranosyl carbon and the glycosidic oxygen atom. The dependence of rate on acidity and the variation of rate with structure are best interpreted in terms of a mechanism involving pyranosyl carbonium ions. In contrast, the acid-catalysed hydrolysis of t-butyl β-D-glucopyranoside involves bond fission between the t-butyl group and the glycosidic oxygen atom, and this reaction is considered to proceed by the formation of an alkyl carbonium ion.

In Part I [1] the acid-catalysed hydrolysis of some simple glucosides was investigated. It was shown that the reactions proceed with hexose–oxygen bond fission and involve pyranosyl carbonium ions as intermediates. The present work, in which a more extensive series of glycosides has been studied, was undertaken with two primary objectives: (*a*) to investigate the anomalously fast hydrolysis of glycosides derived from 2-deoxy-D-glucose and of t-butyl β-D-glucopyranoside, and (*b*) to find an example of glycoside hydrolysis proceeding by the alternative position of bond fission.

Experimental

Materials.—Commercial samples of lactose and maltose had, respectively, $[\alpha]_D^{25}$ +137°, +54° (*c ca.* 2, in H_2O). A commercial sample of *o*-hydroxymethylphenyl β-D-glucopyranoside (salicin) was recrystallised from ethanol, then having $[\alpha]_D^{25}$ −63·5° (*c ca.* 3, in H_2O).

Dry t-butyl alcohol (150 g.), acetobromoglucose (50 g.), silver oxide (50 g.), and ether (400 c.c.) were refluxed together for 45 min. The ether was then removed and the crystals which separated were recrystallised from isopropyl ether. t-Butyl tetra-*O*-acetyl-β-D-glucopyranoside (19 g.) was obtained, with m. p. 143—144°, $[\alpha]_D^{25}$ −12·7° (*c ca.* 1·0, in $CHCl_3$) (Found: C, 53·4; H, 7·0. Calc. for $C_{18}H_{28}O_{10}$: C, 53·5; H, 7·0%). The tetra-acetate was catalytically deacetylated with sodium in anhydrous methanol. After recrystallisation from ethyl acetate, t-butyl β-D-glucopyranoside (6 g.) was obtained with m. p. 163—164°, $[\alpha]_D^{25}$ −19·3° (*c ca.* 1·0, in H_2O) (Found: C, 50·6; H, 8·5. Calc. for $C_{10}H_{20}O_6$: C, 50·8; H, 8·5%). The compound did not reduce Fehling's solution and gave D-glucose on acid-hydrolysis. The infrared spectrum was very similar to that of methyl β-D-glucopyranoside and showed a strong peak at 890 $cm.^{-1}$ characteristic of the β-D-glucose configuration.[2]

Methyl α-2-deoxy-D-glucopyranoside was prepared as described by Stacey and his co-workers.[3,4] It had m. p. 90°, $[\alpha]_D^{22}$ +132° (*c* 1·0, in H_2O) {lit.,[3,4] m. p. 90—92°, $[\alpha]_D^{22}$ +135° (in H_2O)}. Methyl β-2-deoxy-D-glucopyranoside, prepared by the method of Fischer, Bergmann, and Schotte,[5] had m. p. 122°, $[\alpha]_D^{20}$ −45° (*c* 1·0, in H_2O) (lit.,[5] m. p. 122—123°, $[\alpha]_D^{17}$ −48° in H_2O).

Kinetic Methods.—Runs at 25° were followed by determining, at appropriate time intervals, the optical rotatory power of solutions (usually containing *ca.* 2% of the substrate), contained in a jacketed polarimeter tube. The procedure described in Part I [1] was used for runs at higher temperatures.

Isotope Methods.—The positions of bond fission were determined by carrying out the reactions in water enriched in ^{18}O. The detailed procedures for isolating the appropriate

* Part II, *J.*, 1960, 4637.

[1] Bunton, Lewis, Llewellyn, and Vernon, *J.*, 1955, 4419.
[2] Barker, Bourne, Stacey, and Whiffen, *J.*, 1954, 171.
[3] Overend, Stacey, and Stanek, *J.*, 1949, 2841.
[4] Hughes, Overend, and Stacey, *J.*, 1949, 2846.
[5] Fischer, Bergmann, and Schotte, *Ber.*, 1920, **53**, 509.

products were: (*a*) Methyl α-2-deoxy-D-glucopyranoside. As previously described [1] for methyl α-D-glucopyranoside. (*b*) Maltose. A solution (50 c.c.) containing substrate (2·5 g.) in M-perchloric acid was heated at 73° until reaction was complete and then neutralised. Glucosazone, m. p. 201°, was prepared from the products. (*c*) t-Butyl β-D-glucopyranoside. A solution (200 c.c.) containing substrate (25 g.) in 0·92M-perchloric acid was kept at 25° for 47 hr. and then neutralised. The solution was fractionated and the leading fraction collected. Saturation with ammonium sulphate salted out t-butyl alcohol which was dried (Na_2SO_4) and distilled three times from sodium.

Methanol and t-butyl alcohol were pyrolysed to carbon monoxide [1] which was analysed mass spectrometrically. Glucosazone was decomposed by heating it with mercuric chloride, as described by Rittenberg and Ponticorvo,[6] and the carbon dioxide so obtained was analysed mass-spectrometrically.

Results

Kinetic Results.—Good first-order rate coefficients were obtained in all cases and, for each compound, the calculated and observed infinity values agreed within experimental error. The collected first-order rate coefficients (k_1, min.$^{-1}$) are given in Table 1. For each compound, a plot of the logarithm of the first-order rate coefficient against Hammett's acidity function,* H_0, gave a good straight line.

Table 1. *First-order rate coefficients for the hydrolysis of some glycopyranosides.*

o-Hydroxymethylphenyl β-D-glucopyranoside at 72·6°.

$HClO_4$ (M)	0·90	1·50	2·00	2·50	3·00
10^2k_1 (min.$^{-1}$)	0·362	0·88	1·48	2·45	3·73

Lactose at 72·6°.

$HClO_4$ (M)	0·90	1·50	2·00	2·50	3·00
10^2k_1 (min.$^{-1}$)	0·33	0·775	1·31	1·82	2·65

Maltose at 72·6°.

$HClO_4$ (M)	1·50	2·00	2·50	3·00
10^2k_1 (min.$^{-1}$)	0·66	1·16	1·72	2·34

t-Butyl β-D-glucopyranoside at 24·7°.

$HClO_4$ (M)	0·51	1·06	1·44	1·665	2·16	2·70	2·94	3·284
10^2k_1 (min.$^{-1}$)	0·0175	0·0598	0·121	0·187	0·398	0·83	1·21	1·83

Methyl α-2-deoxy-D-glucopyranoside.

Temp.	25·0°	25·0°	25·0°	25·0°	35·0°	44·5°	44·5°
$HClO_4$ (M)	1·04	1·95	0·98[a]	0·495[d]	1·98	0·503	1·01
10^2k_1 (min.$^{-1}$)	0·157	0·599	0·139	0·639	2·89	1·19	3·49
Temp.	44·5°	44·5°	44·5°	44·5°	44·5°	44·5°	44·5°
$HClO_4$ (M)	1·52	2·03	2·11	1·01[b]	2·02[b]	1·03[a]	1·213
10^2k_1 (min.$^{-1}$)	7·41	13·2	16·1	2·87	9·34	3·48	10·80

Methyl β-2-deoxy-D-glucopyranoside.

Temp.	25·0°	25·0°	25·0°	25·0°	25·0°	44·6°	44·6°	44·6°
$HClO_4$ (M)	1·026	1·54	1·98	0·98[a]	0·491[d]	0·532	1·10	1·58
10^2k_1 (min.$^{-1}$)	0·471	1·04	1·75	0·465	1·59	3·46	8·96	18·7

Methyl α-D-glucopyranoside at 44·6°.

$HClO_4$ (M)	4·03
10^2k_1 (min.$^{-1}$)	0·0169

[a] HBr. [b] HCl. [c] D_2O. [d] With 3·5M-$NaClO_4$.

With the two glycosides derived from 2-deoxy-D-glucose, data obtained from experiments in which large concentrations of sodium perchlorate were present and from experiments in which acids other than perchloric acid were used, fitted the Hammett plots quite closely. The values of the slopes (S') of the Hammett plots are given in Table 2. Data for Part I,[1] recalculated

* Values of H_0 as given by Paul and Long.[7]

[6] Rittenberg and Ponticorvo, *Internat. J. Appl. Rad. Isot.*, 1956, **1**, 208.

TABLE 2. *Kinetic parameters for the hydrolysis of glycosides.*

Compound ...	Maltose [a]	Lactose [a]	Salicin [a]	Ph β-G [b]	Me β-G	Bu^t β-G
S'	−0·89	−0·90	−0·95	−0·94	−0·93	−1·30

Compound ...	Me α-G [b]	Ph α-G [c]	Me α-2-deoxy-G [d]	Me β-2-deoxy-G [d]
S'	−0·95	−0·92	−1·04	−0·96
E	33·7	30·8	29·3	27·7
ΔS	+13·8	+13·2	+16·7	+13·7

G = D-Glucopyranoside.
[a] 72·6°. [b] 72·9°. [c] 57·4°. [d] 44·6°. [e] 24·7°.

with the values of H_0 given by Paul and Long,[7] are included. Values of the activation energy E, in kcal. mole^{-1}) and the entropy of activation (ΔS, in cal. mole^{-1} deg.$^{-1}$) have been calculated where the data are sufficient and are also given in Table 2.

Isotope Results.—Table 3 gives the results obtained: N_S and N_M refer to the excess abundance (atom %) of ^{18}O in the solvent and isolated product, respectively; R is the proportion of total reaction at the time of isolation of the product; and Q is the proportion of the reaction apparently proceeding by hexose–oxygen bond fission.

TABLE 3. *Isotope results.*

Compound *	Conditions	R	N_S	N_M	Q
Maltose	2·4M-$HClO_4$, 73°	1·00	1·80	0·05	0·78
Me α-2-deoxy-G	2M-$HClO_4$, 45°	1·00	1·00	0·01	0·99
Bu^t β-G	0·92M-$HClO_4$, 25°	0·734	0·44	0·44	0·00

* G = D-Glucopyranoside.

With maltose, Q is given by $(1 - 8N_M/N_S)$. This arises because N_M refers to the isotopic composition of a product derivative (glucosazone) containing four oxygen atoms, all of which would be isotopically normal if the hydrolysis proceeded by hexose–oxygen bond fission and one of which would be isotopically half enriched if the alternative mode of bond fission occurred. The procedure is not sensitive and the difference between the observed value of Q and unity is probably experimental error, but it may also reflect small amounts of adventitious exchange involving the hydroxyl groups of the substrate or product.

With t-butyl β-D-glucopyranoside a complication arises because the product, t-butyl alcohol, undergoes oxygen exchange at a rate which is of the same order of magnitude as that of the hydrolysis. From Dostrovsky and Klein's data [8] we calculate that the first-order rate coefficient, k_E, for the oxygen exchange of t-butyl alcohol under our conditions (0·92M-$HClO_4$, 25°) is $0{\cdot}82 \times 10^{-4}$ min.$^{-1}$. The isotopic enrichment in the product (N_M/N_S) arising from this exchange alone (*i.e.*, if $Q = 1{\cdot}00$) is then given by the equation: [9]

$$(N_M/N_S)R = 1 - \{[k_1 \exp(-k_E t) - k_E \exp(-k_1 t)]/(k_1 - k_E)\}$$

where k_1 is the first-order rate coefficient for the hydrolysis and the other symobls are defined above. For our conditions ($k_1 = 4{\cdot}7 \times 10^{-4}$ min.,$^{-1}$ $R = 0{\cdot}734$, $t = 2820$ min.), this gives $N_M/N_S = 0{\cdot}13$. Hence, the oxygen exchange of t-butyl alcohol does not account for the observed results and it must be concluded that the hydrolysis of t-butyl β-D-glucopyranoside proceeds with predominant alkyl–oxygen bond fission.

DISCUSSION

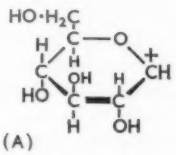
Except for t-butyl β-D-glucopyranoside, the Hammett slopes obtained with the compounds listed in Table 2 are all approximately −1·0.* A more complete kinetic study of the two deoxyglucosides has also shown that the dependence of rate on acidity function is not disturbed by the addition of sodium perchlorate, or by the use of acids other than

* Some of the observed deviation may arise because the rate data and the H_0 values refer, for the most part, to different temperatures.

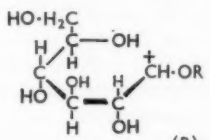
[7] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.
[8] Dostrovsky and Klein, *J.*, 1955, 791.
[9] Bunton, Llewellyn, Oldham, and Vernon, *J.*, 1958, 3574.

perchloric. The hydrolyses of these two compounds and of the methyl D-glucopyranosides have been found to involve large, positive entropies of activation, characteristic of acid-catalysed reactions proceeding by the *A*1 mechanism.[10] The large deuterium isotope effect (k_{D_2O}/k_{H_2O} = 2·5, 1·2M-$HClO_4$, 44·6°) observed with methyl α-2-deoxy-D-glucopyranoside, similar in magnitude to those reported for the acid-catalysed hydrolysis of sucrose and of acetals,[11] is also consistent with the *A*1 mechanism. The evidence suggests, therefore, that there is a common mechanism of hydrolysis of all the glycosides (except, for the moment, t-butyl β-D-glucopyranoside) and that this involves the rate-determining formation of carbonium ions. In Part I, it was shown that hydrolysis of phenyl and methyl D-glucopyranosides proceeds with hexose–oxygen bond fission: in the present work, the same result has been obtained with maltose and with methyl α-2-deoxy-D-glucopyranoside. By reasonable inference, the hydrolysis of lactose, salicin, and methyl β-2-deoxy-D-glucopyranoside may be assumed to follow the same course.

As previously pointed out,[1] some ambiguity exists about the structure of the carbonium ions formed from glycosides by hexose–oxygen bond fission. The ions may arise by direct cleavage of the hexose–oxygen bond or by ring opening, giving structures such as (A) and (B), respectively.* Irrespective of this, however, the carbonium-ion mechanism provides an immediate interpretation of the decrease in rate of hydrolysis in passing from the 2-deoxy-D-glucopyranosides to the parent compounds. The inductive effect of the 2-hydroxyl group impedes formation of either carbonium ion (A) or (B). Hydrolyses of

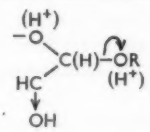


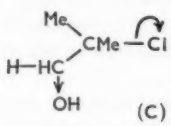
(A)



(B)

t-butyl chloride and 2-chloro-2-methylpropan-1-ol (C) provide appropriate structural comparisons since both these compounds [13,14] are known to react through carbonium ions. The relevant rate data are summarised in Table 4.





(C)

TABLE 4.

Compound	10^5k_1 (min.$^{-1}$)	Ratio (k_H/k_{OH})
Me α-2-deoxy-G [a]	150	2500
Me α-G [a]	0·06	
Bu^{t}Cl [b]	104	103
2-Chloro-2-methylpropan-1-ol	1·01	

G = D-glucopyranoside. [a] M-$HClO_4$, 72·9°, value for the deoxy-compound by extrapolation from 44·6°. [b] In water, 25°, from data in refs. 14 and 15.

It can be seen that a large acceleration occurs in both systems by the removal of a hydroxyl group from a position one atom removed from the reaction centre. The effect

* Evidence derived from the stereochemical course of the reactions and from studies of the oxygen-isotope effect will be presented in a later paper in favour of the view that the reactions actually involve the cyclic ion (A).[12]

[10] Long, Pritchard, and Stafford, *J. Amer. Chem. Soc.*, 1957, **79**, 2362.
[11] Wiberg, *Chem. Rev.*, 1955, **55**, 713.
[12] Banks, Meinwald, Rhind-Tutt, and Sheft, unpublished experiments.
[13] Swain, Cardin, and Ketley, *J. Amer. Chem. Soc.*, 1955, **77**, 934.
[14] Ley and Vernon, *J.*, 1957, 3256.

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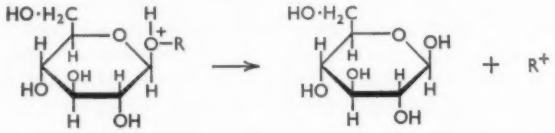
is larger in the sugar compounds, perhaps because the inductive effect of the hydroxyl group impedes both the formation of the conjugate acid and its breakdown into the carbonium ion.*



The hydrolysis of t-butyl β-D-glucopyranoside is much faster than that of the corresponding methyl compound (*ca.* 1000 in M-$HClO_4$, 25°). This larger rate difference becomes intelligible, however, because of the discovery that the hydrolysis of the former compound involves alkyl–oxygen bond fission. This is the first known example of this type of reaction in the glycoside series. The mechanism must involve the production of the alkyl carbonium ion ($R^+ = Bu^{t+}$), and will presumably occur in any glycoside for which the stability of R^+ is greater than that of the glycopyranosyl carbonium ion. Consistently, the reaction rate is dependent on H_0. The Hammett slope, however, is greater than unity and significantly different from the values observed with the glycosides hydrolysing with hexose–oxygen bond fission. This difference in Hammett slope is difficult to interpret. However, stereochemical studies of nucleophilic substitution in tetra-*O*-methyl-D-glucopyranosyl chlorides (Part II) and of the methanolysis of glycosides [12] leads to the conclusion that, in the D-glucose series, carbonium-ion reactions involve transition states in which the nucleophile is well orientated and at no large distance from the reaction centre. For steric reasons, substitution at the t-butyl centre presumably involves a transition state in which the nucleophile is more remote.

Other reactions which are known to involve transition states with well orientated nucleophiles include the acid-catalysed opening of epoxides [15] and the acid-catalysed oxygen exchange of s-butyl alcohol.[16] For both reactions the values of the Hammett slopes are near to unity. It may be that this type of carbonium-ion reaction is a distinct class and is characterised by, among other things, a simple dependence of rate on h_0. In this connection, it would be interesting to have the appropriate data for the D-mannopyranosides since, for these compounds, the evidence suggests (Part II) that the nucleophile cannot approach closely to the reaction centre in the transition state.

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* Conformational effects may also be important with the pyranosides. However, the inductive effect of the hydroxyl group must produce an effect in the observed direction and, since no quantitative estimate can be given, the part played by conformational differences must remain uncertain.

[15] Pritchard and Long, *J. Amer. Chem. Soc.*, 1956, **78**, 2667.
[16] Bunton and Llewellyn, *J.*, 1957, 3402.

74. *The Acid–Base Function in Non-aqueous Solution. Part II.*[1] *The Equilibria of Mono-, Di-, and Tri-n-butylamine with 2,4-Dinitrophenol in Several Aprotic Solvents.*

By John W. Bayles and A. F. Taylor.

In the solvents fluorobenzene, chlorobenzene, bromobenzene, benzene, toluene, anisole, and di-n-butyl ether, the three amines mono-, di-, and tri-n-butylamine (B) react with 2,4-dinitrophenol (HA) to give equilibria of the type, $B + HA \rightleftharpoons BHA$. The equilibrium constants have been determined spectrophotometrically in the temperature range 20—60° and are expressed as changes in standard Gibbs free energies, enthalpies, and entropies.

The results demonstrate that the order of basic strength ($-\Delta G°$) found in chlorobenzene [1] (mono- < di- < tri-n-butylamine) is preserved only in the halogenated benzenes. For limited groups of systems the relation between entropy and enthalpy of reaction is linear. The factors which determine deviations from this relation are discussed, and some consideration is given to the effect of the solvent on the absolute values of the thermodynamic functions measured.

In Part I [1] of this series, the following conclusions were reached: (*a*) In chlorobenzene solution the reaction occurring between an amine, B (mono-, di-, or tri-n-butylamine), and 2,4-dinitrophenol, AH, is of the form

$$B + HA \rightleftharpoons BHA \quad . . . . . (I)$$

(*b*) The ultraviolet absorption spectra of these solutions indicate that the nitrophenol is ionized in much the same way as in water, though because of (*a*) it is always associated through a hydrogen bond with the amine cation. (*c*) The electron-inductive effect of alkyl groups is sufficient to explain the acid–base strength of the amines relatively to the nitrophenol, and steric effects are not important.

The investigation reported in this Part greatly extends our range of solvents, and we find confirmation of the principles (*a*) and (*b*) above. We find now, however, that the order of basic strength in the solvents treated in this Part is not simply related to the electron-inductive effect, and we cannot draw definite conclusions yet about the magnitude of the separate influences of this effect in comparison with solvent and steric factors. Some general conclusions are however possible, and it is becoming clear, not only from our own work, but also from that of other investigators,[2] that the salient differences between the behaviour of proton-transfer equilibria in water and in aprotic solvents are due to the different contributions made by enthalpies and entropies of solvation. In their study of the equilibria between amines and 2,4-dinitrophenol Pearson and Vogelsong [3] measured equilibrium constants at one temperature only, so that it is not possible to assess the varying contributions of enthalpy and entropy terms to the overall free energy of reaction. We have studied both these factors for the reactions of the three n-butylamines with 2,4-dinitrophenol in a set of solvents; where direct comparison with their results is possible agreement is satisfactory, but it also becomes apparent that a detailed explanation of these reactions can only be undertaken when both $\Delta H°$ and $\Delta S°$ are available for study.

Experimental

Reagents.—2,4-Dinitrophenol was treated as described in Part I. Mono-, di-, and tri-n-butylamine were products of Imperial Chemical Industries Limited and were dried over sodium wire; otherwise they were treated as described in Part I. Benzene (Hopkin and Williams,

[1] Part I, Bayles and Chetwyn, *J.*, 1958, 2328.
[2] (*a*) Laidler, *Trans. Faraday Soc.*, 1959, **55**, 1725; (*b*) Mortimer and Laidler, *ibid.*, p. 1731; (*c*) Papée, Canady, Zawidzki, and Laidler, *ibid.*, p. 1734; (*d*) Zawidzki, Papée, Canady, and Laidler, *ibid.*, p. 1738; (*e*) Zawidzki, Papée, and Laidler, *ibid.*, p. 1743.
[3] Pearson and Vogelsong, *J. Amer. Chem. Soc.*, 1958, **80**, 1038.

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G.P.R. grade), anisole and bromobenzene (B.D.H. Laboratory Reagent), and toluene (B.D.H. sulphur-free) were distilled, dried (P_2O_5; 2—5 days), and then fractionated. Di-n-butyl ether (B.D.H. Laboratory Reagent) was dried (KOH), distilled in a stream of dry nitrogen, refluxed in nitrogen over sodium wire (5 hr.), then fractionated from the sodium in a stream of dry nitrogen. Solvents were tested for neutrality with Bromophenol Blue, and their aqueous extracts with Bromothymol Blue in a manner similar to that described in Part I for chlorobenzene. Di-n-butyl ether will pass these tests only if distilled in an atmosphere of nitrogen.

Apparatus and Solutions.—The glassware and optical cells were baked for at least 2 hr. at 150°, cooled in a stream of dry air, and used immediately.

The spectrophotometer and light-absorption cells, all thermostatically controlled, have been described in Part I. The side-arm of the cells was drawn to a wide-bore capillary before filling; the cells were filled from a capillary pipette provided with a rubber teat, and the side-arm was then sealed off in a small flame. Spectra at room temperature were measured on a Unicam S.P. 500 spectrophotometer, and at higher temperatures on the temperature-controlled spectrophotometer.

Solutions were made up by weight as described in Part I, and the same routine of measurement was used. Errors arising from the preparation of the initial solutions were detected since always at least two independent sets of primary solutions were made.

Strengths of Solutions for Measurement.—The spectrophotometric method is most accurate when the optical densities being measured are in the region 1·0—0·1. To make use of this, solutions were prepared at room temperature according to the following plan:

First a solution was found whose molal ratio of amine to nitrophenol was approximately 1 : 1, and whose optical density was about 0·5.

Then two other solutions were prepared with this ratio approximately 2 : 1 and 1 : 2 respectively, both having an optical density of about 0·5.

Finally two solutions with the molal ratio 1 : 1 were prepared, with optical densities of 0·2—0·3 and 0·8—1·0 severally. The optical density of all these solutions over the temperature range 20—60° then falls within the practicable range of measurement, and, in the present systems, equilibria for which the extent of reaction was either too large or too small were avoided.

Results

Units.—As indicated in the preceding section, solutions were made up by weight. Concentrations are expressed in molalities, m, since this interposes a minimum of arithmetic between the experimental quantities and the figures quoted.

Extinction Coefficients.—Extinction coefficients for the complexes BHA in the various solvents were found by determining the limit reached by the quotient D_{410}/m_{AH} for given m_{AH} (where AH = nitrophenol) as the concentration of added base is increased. An experimental graph of this quotient against m_B (B = amine) is given in Part I where the solvent is chloro-

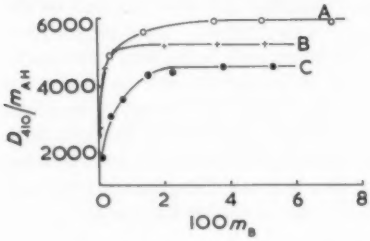

FIG. 1. *The apparent molal extinction coefficient of* 2,4-*dinitrophenol* (AH) *in di-n-butyl ether solutions containing various molalities,* m_B, *of amines. The added amine is* (A) *mono-n-butylamine,* (B) *di-n-butylamine, and* (C) *tri-n-butylamine.*

benzene, and B is either mono-, di-, or tri-n-butylamine. Of the solvents under discussion here, dibutyl ether causes the greatest difference in behaviour of the amine–nitrophenol systems from that in chlorobenzene, and we show therefore in Fig. 1 the experimental graph for the system in dibutyl ether as solvent, and tabulate in Table 1 the values of ε_{410} in all the solvents. The limiting value is written $\varepsilon_{mT\lambda}$ for an experiment conducted at room temperature, T, and wavelength λ (mμ).

Un-ionized 2,4-dinitrophenol has a small but significant extinction coefficient at 410 mμ. This is obtained by measuring the optical density, D_{410}, at known molality and temperature,

t, in the presence of 10^{-2}m-chloroacetic acid to repress any ionization of the nitrophenol by the solvent. Chloroacetic acid does not absorb light at this wavelength. This extinction coefficient is written $\varepsilon'_{mT\lambda}$, and, in its molar form, ε'_{λ}, is also given in Table 1, column 5.

TABLE 1. *Molar extinction coefficients of 2,4-dinitrophenol at 410 mμ.*

In excess:	$Bu^n \cdot NH_2$	Bu^n_2NH	Bu^n_3N	$CH_2Cl \cdot CO_2H$
Fluorobenzene	9939	8965	8780	24
Chlorobenzene	9600	8400	8400	31·6
Bromobenzene	10,020	7840	8710	40·1
Benzene	7040	6180	8530	33·4
Toluene	8700	6210	6880	42·5
Anisole	10,100	8650	9060	137
Di-n-butyl ether	7700	6770	5900	10·2

In dilute solutions containing two light-absorbing species, AHB and AH, we have, at temperature T:

$$D_\lambda = m_{AHB}\varepsilon_{mT\lambda} + m_{AH}\varepsilon'_{mT\lambda}$$

i.e.,

$$m_{AHB} = \frac{D_\lambda - (m_{AH} + m_{AHB})\,\varepsilon'_{mT\lambda}}{\varepsilon_{mT\lambda} - \varepsilon'_{mT\lambda}}$$

where $m_{AH} + m_{AHB}$ is the stoicheiometric molality of 2,4-dinitrophenol in the solution.

Since the molality m of a dilute solution can be equated to the quotient of its molar concentration c by the density of the solvent, ρ_T, we have:

$$\frac{\varepsilon_{mT\lambda}}{\rho_T} = \frac{1}{\rho_T}\frac{D_\lambda}{m_{AHB}} = \frac{D_\lambda}{c_{AHB}} = \varepsilon_\lambda.$$

The molar extinction coefficient ε_λ is independent of temperature, so,

$$\frac{\varepsilon_{mT\lambda}}{\rho_T} = \frac{\varepsilon_{mt\lambda}}{\rho_t}$$

and therefore,

$$\varepsilon_{mT\lambda} \simeq \varepsilon_{mt\lambda}[1 + \alpha(T - t)]$$

where α is the volume coefficient of expansion of the solvent, obtained from the temperature variation of density, and the approximation is acceptable because $\alpha(T - t)$ is small compared with unity. Similarly,

$$\varepsilon'_{mT\lambda} \simeq \varepsilon'_{mt\lambda}[1 + \alpha(t - T)]$$

TABLE 2. *Experimental results for the system, amine + 2,4-dinitrophenol in anisole.*

Mono-n-butylamine:				Di-n-butylamine:				Tri-n-butylamine:			
10^4m_{AH}	10^4m_B	Temp.	D_{410}	10^4m_{AH}	10^4m_B	Temp.	D_{410}	10^4m_{AH}	10^4m_B	Temp.	D_{410}
2·717	2·709	21·5°	0·360	1·372	1·375	20·0°	0·440	1·760	2·082	10·5°	0·810
2·717	2·709	36·5	0·170	1·372	1·375	19·0	0·445	1·760	2·082	35·0	0·335
2·717	2·709	49·0	0·100	1·372	1·375	31·0	0·270	1·760	2·082	48·0	0·180
2·717	2·709	57·5	0·075	1·372	1·375	49·0	0·125	1·760	2·082	57·5	0·120
				1·372	1·375	57·0	0·080				
2·920	5·124	21·0	0·650					1·290	1·187	17·0	0·350
2·920	5·124	34·5	0·335	1·820	1·129	23·0	0·430	1·290	1·187	35·0	0·165
2·920	5·124	47·5	0·185	1·820	1·129	18·0	0·510	1·290	1·187	48·0	0·090
2·920	5·124	57·5	0·125	1·820	1·129	31·5	0·305	1·290	1·187	57·0	0·060
				1·820	1·129	49·0	0·140				
3·840	3·430	22·0	0·630	1·820	1·129	57·0	0·090	1·429	2·944	18·0	0·670
3·840	3·430	35·0	0·330					1·429	2·944	35·0	0·360
3·840	3·430	47·5	0·190	0·869	1·827	23·0	0·340	1·429	2·944	48·0	0·200
3·840	3·430	57·5	0·130	0·869	1·827	20·0	0·376	1·429	2·944	57·5	0·125
				0·869	1·827	32·0	0·230				
5·985	2·854	22·0	0·750	0·869	1·827	49·0	0·100	2·821	1·405	19·5	0·605
5·985	2·854	35·0	0·420	0·869	1·827	57·0	0·065	2·821	1·405	35·5	0·360
5·985	2·854	47·5	0·250					2·821	1·405	48·0	0·205
5·985	2·854	57·5	0·175	2·850	2·561	24·0	1·080	2·821	1·405	57·0	0·140
				2·850	2·561	21·0	1·080				
5·601	4·751	23·5	1·010	2·850	2·561	32·5	0·790	2·806	2·788	20·0	1·050
5·601	4·751	35·0	0·595	2·850	2·561	49·0	0·410	2·806	2·788	35·5	0·600
5·601	4·751	47·5	0·345	2·850	2·561	57·0	0·280	2·806	2·788	48·5	0·350
5·601	4·751	57·5	0·235					2·806	2·788	57·5	0·235

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Thus the expression for m_{AHB} becomes,

$$m_{AHB} = \frac{D_\lambda - (m_{AH} + m_{AHB})\varepsilon'_{mt\lambda}[1 + \alpha(t - T)]}{\varepsilon_{mT\lambda}[1 + \alpha(T - T)] - \varepsilon'_{mt\lambda}[1 + \alpha(t - T)]}$$

All the quantities on the right-hand side of this expression are experimentally obtainable, and this is the form in which the calculation was handled by the computer. The experimental procedure is to measure the molal extinction coefficients of both forms of the nitrophenol (AHB and AH) at the prevailing room temperatures, T and t respectively, and then to use the above expression to obtain m_{AHB} in working solutions at temperature T.

Equilibrium Constants and Thermodynamic Quantities.—The equilibrium constants have been quoted as mole fractional dimensionless quantities, K_x, by multiplying the molal constant K_m by $1000/M$, M being the molecular weight of the solvent. This is necessary because there is one less product molecule than there are reactant molecules. By using this system, we allow for the varying number of moles of solvent per kg. when we make comparisons between thermodynamic quantities obtained in different solvents. The thermodynamic functions are calculated from:

$$\Delta G^\circ = -RT \ln K_x;\ \Delta H^\circ = -R\,\partial \ln K_x/\partial T^{-1};\ \Delta S^\circ = (\Delta H^\circ - \Delta G^\circ)/T.$$

TABLE 3. *Thermodynamic functions for the reaction between some amines and 2,4-dinitrophenol in various solvents.*

Solvent	n-Butylamine	$-\Delta G^\circ_{298}$ (kcal. mole^{-1})			$-\Delta H^\circ_{298}$ (kcal. mole^{-1})			$-\Delta S^\circ_{298}$ (cal. deg.$^{-1}$ mole^{-1})		
Chlorobenzene	Mono-	4·38 ±0·01			11·80 ±0·27			24·9 ±0·9		
	Di-		5·87 ±0·01			11·89 ±0·14			20·2 ±0·5	
	Tri-			6·39 ±0·01			14·16 ±0·23			26·1 ±0·8
Fluorobenzene	Mono-	4·19 ±0·01			13·23 ±0·1			30·3 ±0·4		
	Di-		5·96 ±0·01			12·72 ±0·1			22·6 ±0·5	
	Tri-			6·33 ±0·01			13·81 ±0·1			25·1 ±0·4
Bromobenzene	Mono-	4·06 ±0·01			13·23 ±0·2			30·8 ±0·7		
	Di-		6·08 ±0·01			12·91 ±0·2			22·9 ±0·7	
	Tri-			6·33 ±0·01			13·49 ±0·2			24·0 ±0·7
Benzene	Mono-	4·04 ±0·01			11·86 ±0·1			26·2 ±0·5		
	Di-		5·59 ±0·01			13·13 ±0·1			25·3 ±0·4	
	Tri-			5·28 ±0·1			11·97 ±0·06			22·4 ±0·2
Toluene	Mono-	3·81 ±0·01			11·81 ±0·2			26·8 ±0·5		
	Di-		5·35 ±0·01			13·04 ±0·1			25·8 ±0·4	
	Tri-			5·00 ±0·01			11·71 ±0·1			22·5 ±0·3
Anisole	Mono-	4·97 ±0·01			12·11 ±0·1			24·0 ±0·4		
	Di-		6·31 ±0·01			13·75 ±0·1			24·9 ±0·5	
	Tri-			6·03 ±0·01			12·57 ±0·1			21·9 ±0·2
Dibutyl ether	Mono-	5·46 ±0·01			15·39 ±0·18			33·3 ±0·6		
	Di-		5·74 ±0·01			15·22 ±0·09			31·8 ±0·3	
	Tri-			4·57 ±0·01			11·24 ±0·1			22·4 ±0·4

An example of the experimental results is given in Table 2, and the derived thermodynamic quantities for all systems studied are given in Table 3. The errors given are probable errors, arrived at by the standard statistical manipulation of deviations, and the thermodynamic quantities are the result of a least-squares procedure on the variables ln K and T^{-1}. The calculations have been programmed for the Zebra electronic digital computer using actual weighings, optical densities, temperatures, molecular weights, and coefficients of expansion as input variables.

We have checked that in each system studied the relation between $m_B m_{AH}$ and m_{BHA} at 25° is linear. The graphs showing this are all similar to Fig. 6 of Part I, and an example may readily be constructed from Table 2.

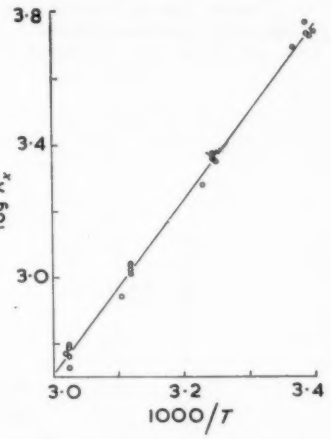

FIG. 2. *The relation between* $\log_{10} K_x$ *and* T^{-1}, *where* K_x *is the equilibrium constant (mole fraction scale) for the equilibrium,* B + HA $\rightleftharpoons$ BHA, *in which* HA *is 2,4-dinitrophenol, and* B *is mono-n-butylamine in anisole solution.*

The magnitude of the experimental scatter in terms of the quoted probable erros can also be seen by comparing Fig. 2 with the tabulated results. In this respect the system mono-n-butylamine + 2,4-dinitrophenol in anisole is typical.

DISCUSSION

In this discussion, the results for the systems mono-, di-, and tri-n-butylamine in equilibrium with 2,4-dinitrophenol in chlorobenzene are based on the experimental results of Part I, but they have been recalculated by the method given above to allow for the small extinction coefficient of AH in chlorobenzene at 410 mμ. This is given in Table 1.

General Principles.—The thermodynamic quantities associated with the type of reaction, B + HA $\rightleftharpoons$ BHA, depend on a rather complex group of influences and, though we shall not make use of all of them in the discussion that follows, it may be helpful to attempt a specification at this stage.

(*a*) Valency force. This will not depend on the solvent, and will increase as the total electron-inductive effect of alkyl groups on nitrogen increases. It will by itself cause tertiary amines to have more negative values of $\Delta G°$ (*i.e.*, be stronger bases) than secondary, and secondary to be stronger than primary, so long as the alkyl groups concerned all have an electron-donating effect. This contribution to the measured thermodynamic quantities may be represented for convenience by making use of an operator symbol Δ_q. We may expect that Δ_q will always make a negative contribution to $\Delta H°$ and $\Delta S°$ and we also expect that the contribution to $\Delta S°$ will be proportional to the effect on $\Delta H°$ [*i.e.*, $\Delta_q(\Delta S°) = a\Delta_q(\Delta H°)$] because the stronger the bond between AH and B, the less free to rotate will the participants be when combined.

(*b*) Other solvent-independent factors. Among these may be mentioned:

(i) The dipole analogue of the Born charging in ionic systems. This will depend on the dimensions of AH and B, and on the length of the AHB bond. We do not at present

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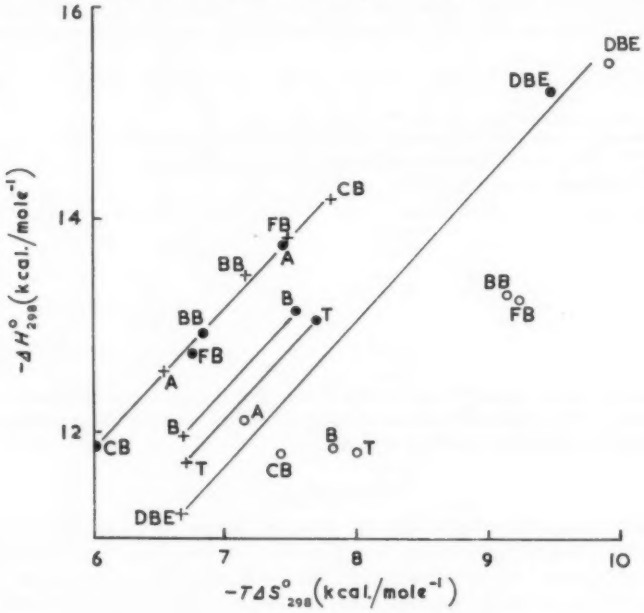
consider that this effect will show sufficient variation between the systems we study to be capable of analysis.

(ii) The large negative contribution to $\Delta S°$ which may be thought of as arising from the simple fact that two independently rotating molecules join to form one, with the consequent limitation on the translation–rotation factors in the partition coefficient of the product molecule as compared with those of the two reactant molecules.

(iii) The statistical effect. In comparing entropies of reactions involving amines with

FIG. 3. *The relation between standard enthalpy and entropy of the reaction* B + HA $\rightleftharpoons$ BHA *at* 25° *in various solvents.* HA *is* 2,4-*dinitrophenol.* B *is mono-n-butylamine for* ○, *di-n-butylamine for* ●, *and tri-n-butylamine for* +. *Point labels for solvent are*: A *anisole*, B *benzene*, BB *bromobenzene*, CB *chlorobenzene*, FB *fluorobenzene*, DBE *di-n-butyl ether*, T *toluene.*



more than one functional amino-group per molecule, we should consider $\Delta S° + \boldsymbol{R} \ln n$ where n is the number of functional groups per molecule. This is unity in all systems in the present work.

(*c*) Solvent interactions. It has been suggested that the peculiar order of basic strength exhibited in water by amines arises because the aminium ions are solvated to an extent dependent on the number of hydrogen atoms attached to the nitrogen atom, and that this effect is opposite to the Δ_q effect above. We may conveniently represent the overall solvent effect by Δ_s.

The Relation between Enthalpy and Entropy of Reaction.—We have looked for the proportionality between $\Delta H°$ and $\Delta S°$ suggested in (*a*) above, and in Fig. 3 it is seen that a relation of this kind holds for the secondary and tertiary amines in the halogenated benzenes and in anisole. Deviations from the line are all on the side of high entropy-loss, or low enthalpy-loss. We prefer to explain them in terms of high entropy-loss because in this type of solvent it seems rather unlikely that the enthalpy of solvation, $\Delta_s(\Delta H)$, will be very significant.

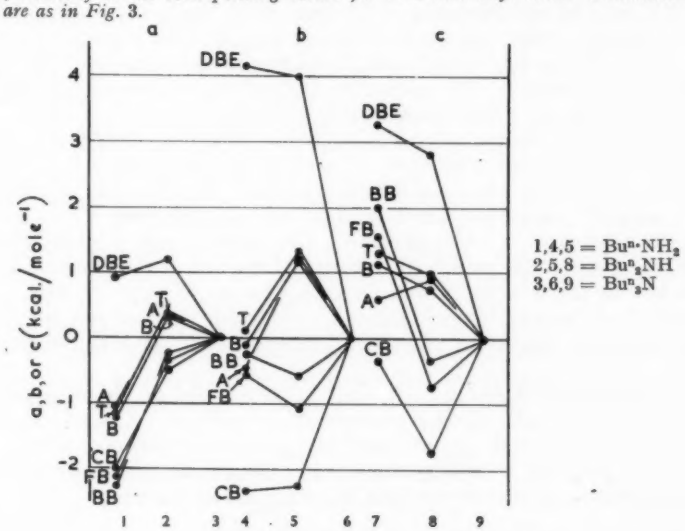
We have also drawn tentative lines through the points for the secondary–tertiary pair

of amines in benzene and toluene showing that these amines in these solvents can be solvated to an extent dependent on the solvent but not on the amine type. One may also suggest that all three amines are affected by solvation to the same extent in dibutyl ether.

The points for mono-n-butylamine show that equilibria involving this amine are very sensitive to solvent, and we believe this to be caused by the protons attached to nitrogen but not involved in the hydrogen bond to the phenolic oxygen atom. If this view is correct, then another conclusion to be drawn from Fig. 3 is that it is necessary for there to be two such hydrogen atoms for solvent-specific abnormalities of this kind to appear.

Treatment of Properties relatively to Those of Tri-n-butylamine.—The evidence of the last paragraph points to a way of considering the behaviour of the thermodynamic quantities in reactions of the type (1). We have calculated the difference in the $-\Delta G°$, $-\Delta H°$,

FIG. 4. (a) $-\Delta G°_{298}$, (b) $-\Delta H°_{298}$, (c) $-T\Delta S°_{298}$ *for the reaction* B + HA $\rightleftharpoons$ BHA *in various solvents, relatively to the corresponding values for* B = *tri-n-butylamine. Point-labels to indicate solvent are as in Fig.* 3.



$-T\Delta S°$ values for mono- and di-n-butylamine as compared with the value for tri-n-butylamine, and plotted these relative values as ordinates against the amines spaced uniformly on a horizontal scale.

It is at once apparent from Fig. 4a that $-\Delta G°$ increases in all solvents when di-n-butylamine replaces mono-n-butylamine in reaction (1). The increase in $-\Delta G°$ on replacing di-n-butylamine by tri-n-butylamine is never as great as this, and in some cases (dibutyl ether, toluene, benzene, anisole) becomes negative. In view of the behaviour of $-\Delta H°$ and $-\Delta S°$ which will next be discussed, we think that there is no simple explanation of this. Laidler [2a] has recently come to the same conclusion in connection with related equilibria in water for which, however, the detailed explanations are not applicable to these systems.

As has already been mentioned, the inductive effect of alkyl groups must make a positive contribution primarily to the enthalpy loss in these reactions, and therefore if this were the only effect, all traces in Fig. 4b would coincide to give one line, both legs of which would have a positive slope. Both parts of the trace for amines in chlorobenzene do have a positive slope, and we suspect that in this solvent there is a minimum of disturbance to the

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simple behaviour. Chlorobenzene is a solvent whose dipole moment is not large (1·55 D) and in which the benzene ring is depleted of electrons inductively so that it will not be readily polarized. Bromobenzene and fluorobenzene are similar to chlorobenzene on both these counts, but the more abnormal behaviour of mono-n-butylamine prevents even the approximation to simple behaviour which is seen in chlorobenzene.

At the other extreme of behaviour is the solvent di-n-butyl ether. In this solvent there is a very high loss of both entropy and enthalpy for the reactions of the primary and secondary amine relatively to the tertiary (Figs. 4b and 4c). This is most probably because the exposed dipole of the ether has a greater affinity for the dipolar B^+HA^- than for either the amine or the nitrophenol molecules.

The two effects, separately dominant in chlorobenzene and dibutyl ether, operate together and contribute nearly equally to the behaviour of the amines in the other solvents. The result is that in toluene, anisole, and benzene, the Figs. 4b and 4c show intermediate behaviour between the two extremes. It may seem a little surprising that in benzene which has no dipole moment we should suggest that solvation is stronger than in bromobenzene, but it must be remembered that the molecule of benzene is readily polarized, and that the attachment through polarized π-electrons may be quite strong, with a strength, $\Delta_s(-\Delta G^\circ)$, whose value is determined more by the relatively low entropy loss than by the low enthalpy loss associated with π-electron interactions. These interactions demand little orientational specificity from the attaching molecule.

The System Tri-n-butylamine + 2,4-Dinitrophenol.—We next consider the properties of the tertiary amine in the various solvents. The order of entropy loss in these is, anisole $\simeq$ dibutyl ether = benzene $\simeq$ toluene $<$ bromobenzene $\leqslant$ fluorobenzene $\leqslant$ chlorobenzene. The order of enthalpy loss is, di-n-butyl ether $<$ toluene $<$ benzene $<$ anisole $<$ bromobenzene $<$ fluorobenzene $<$ chlorobenzene. The entropy loss therefore distinguishes between the halogenated benzenes (high values) and the rest of the solvents, and there is no point in writing down orders within these two groups of three solvents. The same grouping may be read into the order of solvents by enthalpy loss, but here one may specify order within the groups because of the more uniform spread of values and smaller probable errors.

We have examined the dependence of $-\Delta G^\circ_{298}$ (all systems) on the reciprocal dielectric constant, D^{-1}, for if the molecular size parameters are constant (*i.e.*, for given AH and B) the electrical contribution to the experimental ΔG°_{298} will be proportional to D^{-1}. Only the results for tri-n-butylamine + 2,4-dinitrophenol in anisole and the halogenated benzenes can be represented by a relation of this kind, for which the equation is

$$-\Delta G^\circ_{298} = 7{\cdot}583 - 6{\cdot}74D^{-1},$$

and the deviations of the points from this line are less than the probable errors quoted in Table 3. The discussion on Fig. 3 led us to suggest that specific solvent interactions could be small for the systems involving di- and tri-n-butylamine in anisole and the halogenated benzenes, so this evidence from the dependence of $-\Delta G^\circ_{298}$ on D^{-1} confirms the interpretation for tri-n-butylamine and confirms the range of solvents. It does, however, cause us to doubt whether the evidence of Fig. 3 alone is reliably indicative of solvation since the results for di-n-butylamine do not obey a D^{-1} relation.

The solvents in which the tri-n-butylamine system does not obey a D^{-1} relation are benzene, toluene, and di-n-butyl ether. The last may be anomalous because of its exposed dipole and because it has no aromatic system. We suggest that benzene and toluene are anomalous because the polarizability of the aromatic electrons is relatively high. In the halogenated benzenes, on the other hand, the inductive effect of the halogen atoms removes this effect.

We thank Imperial Chemical Industries Limited for gifts of chemicals, Messrs. Standard Telephones and Cables (Newport, Mon.) for the gift of time on their Zebra computer, Dr. D.

Rogers of the Physics Department in this College for instruction in the use of Zebra simple code, and the Department of Scientific and Industrial Research for a maintenance allowance to A. F. T.

UNIVERSITY COLLEGE, CARDIFF. [*Received, May 5th,* 1960.]

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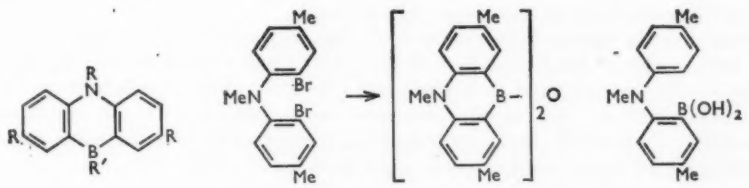
75. *New Heteroaromatic Compounds. Part IX.* Some 10,9-Borazaroanthracenes.*†

By P. M. MAITLIS.

The preparation and properties of a number of 10-substituted 3,6,9-trimethyl-10,9-borazaroanthracenes are described. It is concluded that less aromatic stabilisation occurs in the hetero-ring here than in the 10,9-borazarophenanthrenes.

THE preparation of a number of heteroaromatic molecules containing boron in the ring has been described and some of their properties have been investigated.[1-3] It has been concluded from these that when the boron has oxygen or nitrogen adjacent to it in a six-membered conjugated ring there is considerable stabilisation of that ring owing to the participation in the ground state of structures such as $-^{+}NH{=}B^{-}H-$, and the usual reactivity of the boron is greatly decreased. We therefore investigated systems with non-adjacent heteroatoms in order to find out what effect this has on the stability of the molecule. Derivatives of one such system, 9,10-boroxaroanthracene,[2] have already been reported, but the properties have not yet been fully investigated. Since, however, Dewar and Dietz [1] showed that molecules containing $-O{\cdot}BR-$ groups are less stabilised than molecules containing $-NH{\cdot}BR-$ groups it was decided to investigate the 10,9-borazaroanthracenes [9,10-dihydro-9-aza-10-bora-anthracene] (I; R = R′ = H).

A simple synthesis of the unsubstituted ring system was not feasible; however, since it has been shown that the presence of a methyl group on the nitrogen in the borazarophenanthrenes does not lead to any significant reduction in stability,[3] derivatives of 3,6,9-trimethyl-10,9-borazaroanthracene (I; R = Me) were prepared. The starting material for



(I) (II) (III) (IV)

these compounds was the readily available 2,2′-dibromo-4,4′,*N*-trimethyldiphenylamine [4] (II).

Treatment of the 2,2′-dilithio-derivative from the amine (II) (prepared by use of butyl-lithium) with butyl orthoborate in ether gave, after hydrolysis, a very low yield (12%) of the cyclic compound (III), together with some of the uncyclised boronic acid

* Part VIII, *J. Amer. Chem. Soc.*, 1960, **82**, in the press.
† For this nomenclature see *J.*, 1959, 2728.

[1] Dewar, Kubba, and Pettit, *J.*, 1958, 3073, 3076; Dewar and Kubba, *Tetrahedron*, 1959, **7**, 213; Dewar and Dietz, *J.*, 1959, 2728; 1960, 1344.
[2] Davidson and French, *J.*, 1960, 191.
[3] Maitlis and Dewar, *J. Amer. Chem. Soc.*, in the press.
[4] Weitz and Schwechten, *Ber.*, 1927, **60**, 550; Gilman and Zuech, *J. Org. Chem.*, 1959, **24**, 1394.

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(IV) (12%); the yield of anhydride was increased to 65% by reaction with butyl metaborate in boiling ether for 1 hr. Using the boron trifluoride–ether complex instead of butyl metaborate gave a low yield.

Evidence for the cyclic structure of the product comes from the elemental analysis, which precludes an uncyclised structure, and the ultraviolet spectrum (Fig. 1). The isoconjugate hydrocarbon is unknown so that no direct comparisons can be made; however, the spectrum of the product resembles those of anthracene- and acridine-type compounds, notably in a strong peak at 382 mμ (log ε 3·86) which diphenylamines, *e.g.*, (IV), do not show.

The product, expected to be 10-hydroxy-3,6,9-trimethyl-10,9-borazaroanthracene, is the anhydride (III), as is shown by the carbon analysis, by its insolubility in aqueous sodium hydroxide, and by the absence of a hydroxy peak in the infrared spectrum. The molecular weight found by the Rast method gives an intermediate value (common with compounds of this type), presumably owing to some reaction with the camphor. In ethanolic solution, however, the ethyl ester (I; R = Me, R′ = OEt) exists: in 50% aqueous

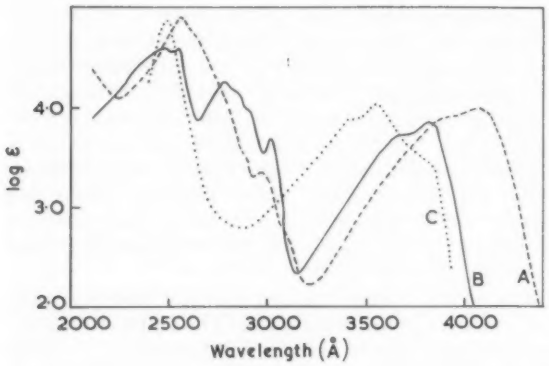


FIG. 1. *Spectra of* (A) *compound* (I; R = Me, R′ = Ph), (B) *compound* (III), *and* (C) *acridine, all in ethanol.*

ethanol the product shows pK_a *ca.* 11·2, a value very close to that obtained for the " hydroxy "-borazaro-naphthalene and -phenanthrene.

Treatment of the dilithiodiphenylamine in ether with dibutyl phenylboronate in ether gave a 10% yield of 3,6,9-trimethyl-10-phenyl-10,9-borazaroanthracene (I; R = Me, R′ = Ph), which was prepared in better yield (77%) by treating a benzene solution of compound (III) with five mol. of phenylmagnesium bromide in ether. Attempts to make the 10-methyl-, 10-n-butyl-, and 10-t-butyl-borazaroanthracene by the same route from compound (III) all failed, only starting material being isolated. Since in each of these cases reaction occurred it must be concluded that the product was lost during the working-up by aerial oxidation, in spite of attempts to avoid it.

Addition of small amounts of alkali to an ethanolic solution of the *B*-hydroxy- or the *B*-phenyl compound caused an immediate change in the ultraviolet spectrum in which the acridine-like spectrum [5] was replaced by a diphenylamine-type spectrum. This was particularly pronounced in the long-wavelength band which entirely disappears in 5% alkali (Figs. 1 and 2). The effect is reversed in both cases on addition of acid. The changes can be explained only by assuming that in alkali the anthracene-type conjugation is interrupted and an adduct of type (V) is formed. An attempt was made to isolate such an adduct by preparing the ethanolamine derivative * which might be expected to have a

* Letsinger and Skoog [6] showed that diarylboronic acids form cyclic adducts of this type with ethanolamine in which the boron is tetrahedral and stabilised by back-co-ordination.

[5] Blout and Corley, *J. Amer. Chem. Soc.*, 1947, **69**, 766.
[6] Letsinger and Skoog, *J. Amer. Chem. Soc.*, 1955, **77**, 2491.

spiro-structure (VI). The ethanolamine derivative from compound (III) was prepared and had absorption in the 2·5—3·5 μ range similar to that of the ethanolamine derivative of diphenylboronous acid; however, the ultraviolet spectrum was identical with that of

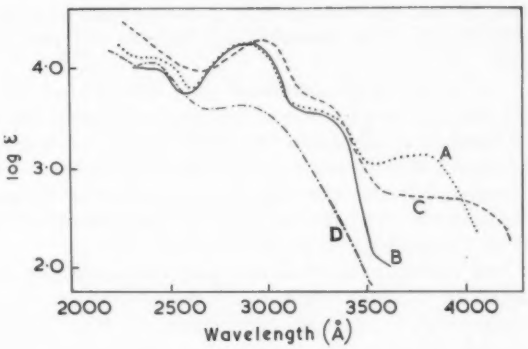


FIG. 2. *Spectra of compound* (III) *in ethanol containing* (A) 0·5% *and* (B) 5% *of* KOH, (C) *compound* (I; R = Me, R′ = Ph) *in ethanol containing* 0·5% *of* KOH, *and* (D) *compound* (IV) *in ethanol.*

the compound (III) in both ethanol and cyclohexane, suggesting that, although perhaps in the solid state structure (VI) is important, in solution the amine is too weak a base to co-ordinate on to the boron. 9-Hydroxy-9,10-boroxaroanthracene [2] showed an analogous reversible shift in the ultraviolet spectrum on the addition of alkali (Fig. 3).

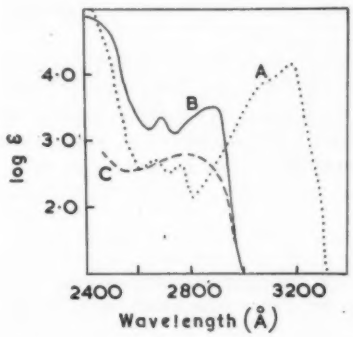
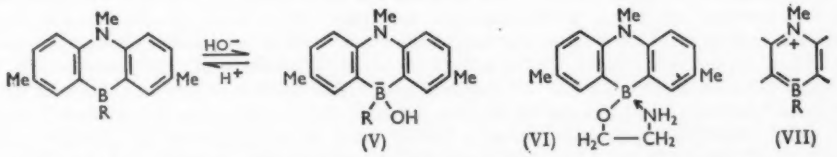


FIG. 3. *Spectra of* 9-*hydroxy*-9,10-*borazaroanthracene* [2] (A) *in ethanol and* (B) *in ethanol containing* ~0·2% *of* NaOH, *and* (C) o-*phenoxyphenylboronc acid in cyclohexane.*[2]

The anhydride (III) could not be brominated without loss of the boron; with two mol. of bromine in acetic acid it gave an 87% yield of 2,2′-dibromo-4,4′,*N*-trimethyldiphenylamine; no boron-containing material could be isolated. Since the borazaroanthracene



(III) is stable in acetic acid under the conditions of the experiment, this must be a case of deboronation by bromine [7] rather than by acetic acid [8] followed by bromination.

[7] Kuivila and Easterbrook, *J. Amer. Chem. Soc.*, 1951, **73**, 4629.
[8] Meerwein, Hinz, Majert, and Sönke, *J. prakt. Chem.*, 1936, **147**, 251; Goubeau, Epple, Ulmschneider, and Lehmann, *Angew. Chem.*, 1955, **67**, 710; Brown and Murray, *J. Amer. Chem. Soc.*, 1959, **81**, 4108.

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The properties of the 10,9-borazaroanthracene system as described above lead to the conclusions (1) that the central ring has some aromatic stabilisation as represented by (VII) [this is supported by the stability of compound (III) towards aerial oxidation and by the acridine-type spectrum of both the *B*-hydroxy- and *B*-phenyl-borazaroanthracene] and (2) that this stabilisation is not as great as in molecules where the heteroatoms are adjacent, as in the borazaro-naphthalenes and -phenanthrenes. Three reactions illustrate this.

(*a*) With alkali compound (III) gives an adduct which does not allow conjugation through the boron, whereas with the naphthalene and the phenanthrene analogues addition of alkali to the *B*-hydroxy-compound causes only a slight bathochromic shift; this would be expected if the anion $>B{\cdot}O^-$ were formed which had the possibility of existing to some extent as $>\overline{B}{=}O$. That this is not an effect of the methyl group attached to the nitrogen has been shown by the fact that the spectrum of 9,10-dimethyl-10,9-borazarophenanthrene is unchanged on addition of alkali.[3]

(*b*) Borazaro-naphthalenes and -phenanthrenes containing alkyl groups attached to boron are relatively stable to aerial oxidation and are only slowly oxidised to the hydroxy-compounds in solution. Preparation of the *B*-alkylborazaroanthracenes has not been possible owing to the (presumed) readiness with which they are oxidised, and even the *B*-phenyl compound is slowly oxidised in ethanolic solution to the anhydride (III). This implies that the boron in this molecule is not greatly stabilised by the nitrogen and that for complete stabilisation a further group must be present which can give the boron some back-co-ordinative stability, such as oxygen or a phenyl.

(*c*) This is the only case hitherto where boron in a heteroaromatic ring is readily removed by a reagent as mild as bromine, and again implies a lack of aromatic stabilisation in the central ring.

This conclusion is not unexpected. Dewar and Lucken [9] showed by nuclear quadrupole resonance studies that conjugative interaction, which is large between chlorine and nitrogen in 2-chloropyridine, is vanishingly small in 4-chloropyridine. By analogy interaction between adjacent nitrogen and boron would be expected to be great, but very much smaller when these atoms are separated by two carbon atoms.

Experimental

Ultraviolet spectra were determined by a Unicam S.P. 500 spectrophotometer for 95% ethanol and cyclohexane solutions. Microanalyses were by Alfred Bernhardt, Max-Planck-Institut für Kohlenforschung, Mülheim, Germany.

Bis-(3,6,9-*trimethyl*-10,9-*borazaro*-10-*anthryl*) *Ether*.—(*a*) An ethereal solution of n-butyllithium (50 ml., 0·06 mole) was added slowly with stirring to an ice-cold solution of 2,2′-dibromo-4,4′,*N*-trimethyldiphenylamine [4] (9·4 g., 0·0255 mole) in ether (50 ml.), under dry, oxygen-free nitrogen. The mixture was stirred at 0° for 2 hr., then n-butyl metaborate (3·3 g., 0·03 mole) in ether (30 ml.) was run in slowly. The mixture was allowed to warm to room temperature and then refluxed for 1 hr. 2N-Hydrochloric acid (200 ml.) was added, the ethereal layer separated, and the acid layer again extracted with ether. The ether solutions were combined, dried ($MgSO_4$), and evaporated, giving a dark oil which on addition of light petroleum (b. p. <40°) gave yellow needles (2·9 g.). Chromatography of the mother liquors on alumina in light petroleum yielded a small amount of starting material (1·7 g., 18%), m. p. and mixed m. p. 101—102°; ether–light petroleum eluted a further 0·2 g. of boron-containing material. The total yield of anhydride was 3·1 g. (65% based on recovered starting material). Crystallisation from benzene–light petroleum (b. p. 100—120°) gave very pale yellow prisms, m. p. 244—245°. Further crystallisation from ether–light petroleum gave colourless material of the same m. p. (Found: C, 79·2; H, 6·7; N, 6·0; B, 5·2%; *M*, 312. $C_{30}H_{20}B_2N_2O$ requires C, 78·95; H, 6·6; N, 6·1; B, 4·8%; *M*, 456).

[9] Dewar and Lucken, *Chem. Soc. Special Publ.*, No. 12, 1958, p. 231.

The *ethanolamine derivative*, obtained by treating the anhydride with ethanolamine in benzene, crystallised in needles, m. p. 223—224° (Found: C, 73·05; H, 7·5; N, 9·95; B, 4·1. $C_{17}H_{21}BN_2O$ requires C, 72·85; H, 7·5; N, 10·0; B, 3·9%).

(*b*) Reaction as above, with half-quantities, but 6·0 g. of butyl orthoborate in ether (30 ml.) and 19 hours' stirring at room temperature, gave a dark oil. With light petroleum this gave first, the anhydride (III) (360 mg., 12%) and then a white solid (400 g.), which on crystallisation from benzene gave 5-*methyl*-2-(N-*methyl*-N-p-*tolylamino*)*phenylboronic acid* (IV), m. p. 165—166° (Found: C, 70·7; H, 7·2; N, 5·4; B, 4·1. $C_{15}H_{18}BNO_2$ requires C, 70·6; H, 7·1; N, 5·5; B, 4·3%).

3,6,9-*Trimethyl*-10-*phenyl*-10,9-*borazaroanthracene*.—(*a*) The reaction was as described under (*b*) above except that dibutyl phenylboronate (4·5 g.) in ether (15 ml.) was used in place of the butyl borate. The brown oily product was chromatographed on alumina in light petroleum (b. p. <40°), to give a small amount of boron-free oil (presumably 4,4′,*N*-trimethyldiphenylamine); addition of ether to the eluant led to a yellow solid (410 mg., 10%) which crystallised from ether–light petroleum as fluorescent yellow needles, m. p. 114—115°; this was 3,6,9-*trimethyl*-10-*phenyl*-10,9-*borazaroanthracene* (Found: C, 84·6; H, 6·9; N, 4·8; B, 4·0%; *M*, 282. $C_{21}H_{20}NB$ requires C, 84·85; H, 6·7; N, 4·7; B, 3·7%; *M*, 297).

(*b*) An ethereal solution (25 ml.) of phenylmagnesium bromide (from bromobenzene, 3·5 g., and magnesium, 0·5 g.) was added with stirring to a solution of the anhydride (III) (1 g.) in benzene (20 ml.). After refluxing for 1 hr. the solution was cooled, hydrolysed with dilute hydrochloric acid, and extracted with ether. The ether extracts were combined, dried, and evaporated. A residue of low-melting yellow solid (1·45 g.) was obtained which on recrystallisation from light petroleum (b. p. 40—60°) gave 3,6,9-trimethyl-10-phenyl-10,9-borazaroanthracene (1·0 g., 77%), m. p. and mixed m. p. 114—115°.

Bromination of the Anhydride (III).—A solution of the anhydride (III) (1·7 g.) in glacial acetic acid (20 ml.) was treated with bromine (0·9 ml., 2·2 mol.) in this acid (10 ml.). The solution became bluish-green, then an oil was precipitated that was redissolved by gentle warming on a steam-bath. After 30 min. the solution was poured into a large excess of water and left overnight. The clear supernatant liquid was then decanted (basification gave no more material) and the solid dissolved in benzene, dried, and recovered. Addition of light petroleum (b. p. 100—120°) gave 2,2′-dibromo-4,4′,*N*-trimethyldiphenylamine (2·4 g., 87%), m. p. 100—102°, mixed m. p. with synthetic material 101·5—103·5°.

An experiment in which the anhydride (III) was left in hot glacial acetic acid solution for 1 hr. and then precipitated gave no significant quantity of boron-free material.

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76. *Phosphonitrilic Derivatives. Part IV.*[1] *The Heats of Formation of the Trimeric and Tetrameric Phosphonitrilic Chlorides.*

By S. B. Hartley, N. L. Paddock, and H. T. Searle.

The heats of formation of trimeric and tetrameric phosphonitrilic chlorides have been determined by combustion; $\Delta H_f°(PNCl_2)_3(c) = -194{\cdot}1$ kcal. mole^{-1}, $\Delta H_f°(PNCl_2)_4(c) = -259{\cdot}2$ kcal. mole^{-1}. The average P–N bond-energy terms of the two compounds are almost identical, that of the tetramer being slightly the higher; both are greater than expected for a single bond.

Comparatively few determinations of the heats of formation of compounds of phosphorus and nitrogen have been reported.[2,3] In this connection, the phosphonitrilic compounds $(PNX_2)_n$ are of special interest in that they are formally unsaturated and possess many of the attributes of aromatic character, the theoretical basis of which has been developed by Craig.[4] The energetics of the cyclic phosphonitrilic skeleton may be studied conveniently with the chlorides, which burn to simple products. The present paper describes the determination, by combustion, of the heats of formation of the trimeric and tetrameric chlorides.

Experimental

Preparation of Compounds.—The trimeric chloride $(PNCl_2)_3$ was prepared from the commercial material by recrystallisation from light petroleum, followed by a double sublimation (m. p. 112·8°). The tetrameric chloride was obtained pure (m. p. 122·8°) and free from a more stable polymorphic form [5] by a double sublimation followed by recrystallisation from benzene at 25°. The crystals were dried *in vacuo* below 25°, the form so obtained being that of known crystal structure.[6] Its crystallographic purity was established by *X*-ray diffraction, and absence of solvent by a combustion experiment in which no carbon dioxide was formed.

Experimental Method.—The calorimeter used was of the standard type (Baird and Tatlock, Ltd.), and incorporated a 300 ml. stainless-steel bomb of the single-valve type. It was modified so as to ensure more exact control of the jacket temperature and more rapid attainment of thermal equilibrium. All combustions were carried out in 30 atm. of oxygen in a dry bomb; water was avoided throughout, since its use in the experiments with the phosphorus compounds would have given products hydrated to an uncertain extent. Temperatures were measured with a mercury-in-glass thermometer which had been calibrated to $\pm 0{\cdot}001°$. The observed temperature rise was corrected in all the experiments by the method of Regnault and Pfaundler. The energy equivalent of the calorimeter was determined (within 0·1%) with benzoic acid (B.D.H. Thermochemical Standard), allowance being made for the formation of nitric acid in its combustion.

All samples were burned in a shallow platinum dish, the amount being adjusted to give a temperature rise of 1·8—2°, with a final temperature in the range 24° ± 1°. Samples were ignited by an electrically heated platinum wire; complete combustion of the phosphonitrilic chlorides was ensured by tying a small fragment of hair to the platinum fuse and allowing it just to touch the surface of the sample.

Combustion Process.—The phosphonitrilic chlorides were found to burn essentially according to the equation:

$$(PNCl_2)_n(c) + \frac{5n}{4}O_2(g) \longrightarrow \frac{n}{4}P_4O_{10}(c) + \frac{n}{2}N_2(g) + nCl_2(g)$$

The solid and the gaseous products of combustion were both analysed; no significant difference (either qualitative or quantitative) could be detected between the products of combustion of

[1] Part III, Chapman, Paddock, Paine, Searle, and Smith, *J.*, 1960, 3608.
[2] Neale and Williams, *J.*, 1956, 422.
[3] Fowell and Mortimer, *J.*, 1959, 2913.
[4] Craig and Paddock, *Nature*, 1958, **181**, 1052; Craig, *J.*, 1959, 997; "Theoretical Organic Chemistry," Butterworths Sci. Publ., London, 1959, p. 20.
[5] Lund, Paddock, Proctor, and Searle, *J.*, 1960, 2542.
[6] Ketelaar and de Vries, *Rec. Trav. chim.*, 1939, **58**, 1081.

the two chlorides. The phosphorus pentoxide was shown by *X*-ray powder photography to be the metastable, hexagonal form. Its heat of formation was taken to be that of a crystalline form of the oxide (probably hexagonal) as determined by Giran [7] and re-interpreted by Rossini *et al.*[8] The small amount of residue insoluble in water (0—0·3% of sample weight) was found to be a highly polymeric form of phosphonitrilic chloride. Its weight was subtracted from the initial sample weight, no correction being made for the heat of polymerisation. In early experiments phosphorous and hypophosphorous acids were determined iodometrically, but the amounts found were too small for accurate estimation. Phosphorus was therefore determined as orthophosphoric acid by the quinoline molybdate method,[9] both before and after oxidation with bromine and nitric acid. The phosphorus recovered in each case was 99·7 ± 0·3% (average of six measurements) and 100·2 ± 0·2% (average of seven measurements); the difference between the two figures was taken as tervalent phosphorus, and a correction applied.

The gaseous reaction product was examined for oxides of nitrogen and of chlorine, for nitrosyl chloride, and for phosphorus oxychloride. The chlorine and other products were frozen out of the bomb gases; no oxide of nitrogen or of chlorine or nitrosyl chloride was detected on infrared spectroscopic examination of the condensed gases, nor was nitrosyl chloride detected, either by its volatility or on absorption of the concentrated bomb gases in alkali. No phosphorus oxychloride was detected after evaporation of the more volatile constituents. A very small amount of nitrogen dioxide was found by absorption on a mixture of silica gel and potassium dichromate in concentrated sulphuric acid,[10] followed by reduction with Devarda's alloy and estimation as ammonia. The quantities found, however, were small (0·002—0·022 g. of NO_2), and an average correction was applied to all the heat measurements. Elemental chlorine was estimated by absorption in alkali, followed by reduction to chloride with sulphur dioxide and determination by Volhard's method. The average recovery was 99·6 ± 0·2% (five measurements). Nitrogen was determined after further absorption of oxygen in sodium dithionite solution. The average recovery was 100·4 ± 0·4% (six measurements).

Heat Measurements.—All thermal quantities are given in terms of the thermochemical calorie (=4·1840 abs. joules). The mean of six measurements of the heat of combustion of the trimeric chloride was 345·3 kcal. mole^{-1}, and of the tetrameric chloride 460·0 kcal. mole^{-1}. These figures were corrected for the small amount of partly burned phosphorus (0·5%) by assuming it to be in the tervalent state, and its heat of oxidation to correspond to the formation of phosphoryl bonds having a bond dissociation energy of 120 kcal. mole^{-1}. The corrections to the evolved heat were +0·90 kcal. mole^{-1} for the trimeric chloride, +1·20 kcal. mole^{-1} for the tetrameric chloride. The presence of nitrogen dioxide (an average of 0·010 g. for an average sample weight of 4·5 g.) necessitated a further correction (+0·12, +0·18 kcal. mole^{-1}), and with the appropriate allowance for the increase in the number of gaseous molecules on combustion (−0·45, −0·60 kcal. mole^{-1}), we find, finally, $\Delta H_c(PNCl_2)_3(c) = -345{\cdot}9$ kcal. mole^{-1}, $\Delta H_c(PNCl_2)_4(c) = -460{\cdot}8$ kcal. mole^{-1}. The accepted value [8] for $\Delta H_f^\circ(P_4O_{10})(c)$ is −720·0 kcal. mole^{-1}, leading to the heats of formation $\Delta H_f^\circ(PNCl_2)_3(c) = -194{\cdot}1$ kcal. mole^{-1}, $\Delta H_f^\circ(PNCl_2)_4(c) = -259{\cdot}2$ kcal. mole^{-1}.

It is necessary to take into account errors (i) in the thermal measurements, (ii) arising from incomplete reaction or inexact knowledge of it, (iii) in the calibration experiments, and (iv) in the heat of formation of phosphorus pentoxide (the reliability of which is not here assessed). The standard deviations of the means of the thermal measurements corrected as described were 0·2, 0·4 kcal. mole^{-1} for the trimer and tetramer. The chemical error is more difficult to estimate, but is probably comparable. For a comparison between the two polymers (one of the main purposes of this paper) no further errors need be considered, and the standard deviations of the mean heats of formation are therefore taken as 0·4, 0·8 kcal. mole^{-1} for this purpose. Inaccuracies in the calibration introduce the further uncertainties 0·3, 0·4 kcal. mole^{-1}.

The heat of sublimation of the trimeric chloride is known [11] (18·2 ± 0·2 kcal. mole^{-1}) but only the heat of vaporisation of the liquid tetrameric chloride [12] (15·5 kcal. mole^{-1}). Its heat of fusion was determined indirectly by measuring its heat of solution in benzene and correcting,

[7] Giran, *Ann. Chim. Phys.*, 1903, **30**, 203.
[8] Rossini *et al.*, National Bureau of Standards, Circular 500, Washington D.C., 1952.
[9] Wilson, *Analyst*, 1951, **76**, 65.
[10] Koshun and Klimova, *Zhur. analit. Khim.*, 1949, **4**, 292.
[11] Steinman, Schirmer, and Audrieth, *J. Amer. Chem. Soc.*, 1942, **64**, 2377.
[12] Moureu and de Ficquelmont, *Compt. rend.*, 1941, **213**, 306.

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by Hildebrand's solubility theory,[13] for the heat of mixing of the two liquids. The calorimeter consisted of a Dewar vessel immersed as completely as possible in a thermostat bath maintained at 25°c. It contained a stirrer, heater coil for calibration, and a Beckmann thermometer capable of being read to within ±0·002°. The powdered chloride was equilibrated at the temperature of the benzene, and mixed rapidly with it. The temperature changes recorded were of the order of −2·4°; small corrections were made for heat losses during the short solution period. The heat of solution at 25° was found to be 7·75 kcal. mole^{-1}; the heat of mixing was calculated to be 0·15 kcal. mole^{-1}, leading to a value for the heat of fusion of 7·60 ± 0·1 kcal. mole^{-1}, and the heat of sublimation of the tetrameric chloride at 25° is therefore assessed at 23·1 ± 0·2 kcal. mole^{-1}. The heats of formation of the two compounds in the vapour phase are, therefore, $\Delta H_f°(PNCl_2)_3(g) = -175·9$ kcal. mole^{-1}, $\Delta H_f°(PNCl_2)_4(g) = -236·1$ kcal. mole^{-1}.

Discussion

The heats of formation of the $PNCl_2$ unit in the gas phase are −58·63 kcal. mole^{-1} for the trimeric chloride, and −59·03 kcal. mole^{-1} for the tetrameric chloride. Energetically, therefore, there is little difference between the two molecules. From the known heats of formation of the gaseous atoms (phosphorus [14] 75·3, nitrogen [15] 112·9, chlorine [16] 28·9 kcal. g.-atom^{-1}) the heats of atomisation may be calculated as 913·9 kcal. mole^{-1} (trimeric chloride) and 1220·1 kcal. mole^{-1} (tetrameric chloride). If, in a particular molecule, all the P–N bonds are assumed equal, and all the P–Cl bonds are assumed equal, the sum of the bond energy terms $\overline{E}$(P–Cl) + $\overline{E}$(P–N) is 152·3 kcal. mole^{-1} for the trimer, 152·5 kcal. mole^{-1} for the tetramer. If $\overline{E}$(P–Cl) can be taken to be the same in both molecules, the difference of 0·2 kcal. can be taken as a measure of the strengthening of the ring bonds in the tetramer as compared with the trimer. The difference is too small compared with its standard deviation (0·12 kcal.) to be considered significant. By contrast, it may be deduced from the heats of combustion in the gas phase of benzene [17] (788·4 kcal. mole^{-1}) and of cyclo-octatetraene [18] (1095·2 kcal. mole^{-1}) that the increase in ring size here entails a decrease in $\overline{E}$(C–C), averaged over all ring bonds, of 2·75 kcal., provided $\overline{E}$(C–H) remains unchanged. This difference demonstrates a clear distinction between the two series of compounds.

The length of the P–Cl bond in trimeric phosphonitrilic chloride [19] is 1·98 Å, and it is therefore reasonable to take $\overline{E}$(P–Cl) as 80 kcal. mole^{-1}, the value estimated by Neale and Williams [20] for phosphorus oxychloride, in which the length of the P–Cl bond [21] is 1·99 Å. For the trimeric and tetrameric chlorides, we therefore obtain $\overline{E}$(P–N) = 72·3, 72·5 kcal. mole^{-1} respectively. Both values are higher than expected for a single bond, a value of 66·8 kcal. mole^{-1} having been obtained by Fowell and Mortimer [3] for $\overline{E}$(P–N) in trisdiethylaminophosphine. The difference seems, however, to be less than would be expected from the difference in the lengths of the P–N bonds in the trimer chloride [19] (1·60 Å) and the phosphoramidate ion [22] $NH_2PO_3^{2-}$ (1·78 Å).

We are grateful to J. K. Jacques for help in measuring the heats of solution of the tetrameric chloride, and to A. C. Chapman, A. Wilson, and F. R. Tromans for infrared and *X*-ray analyses.

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Oldbury, Birmingham.

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[13] Hildebrand and Scott, "The Solubility of Non-Electrolytes," Reinhold Publ. Corp., New York, 3rd edn., 1950.
[14] Cottrell, "The Strengths of Chemical Bonds," Butterworths Sci. Publ., London, 2nd edn., 1958, p. 162.
[15] Cottrell, ref. 13, p. 160.
[16] Cottrell, ref. 13, p. 165.
[17] Prosen, Gilmont, and Rossini, *J. Res. Nat. Bur. Stand.*, 1945, **34**, 65.
[18] Springall and White, *Trans. Faraday Soc.*, 1954, **50**, 815.
[19] Wilson and Carroll, *J.*, 1960, 2548.
[20] Neale and Williams, *J.*, 1955, 2485.
[21] Bell, Heisler, Tannenbaum, and Goldenson, *J. Amer. Chem. Soc.*, 1954, **76**, 5185.
[22] Hobbs, Corbridge, and Raistrick, *Acta Cryst.*, 1953, **6**, 621.

77. *The Speed of Analysis by Gas Chromatography.*

By John H. Knox.

Expressions are derived for the minimum possible analysis times on capillary and packed columns in terms of the separation S and the column-pressure drop Δp. It is shown that there is little to choose between the speed of packed and of capillary columns.

There is still some difference of opinion as to whether analysis by gas chromatography is faster on a packed or on a capillary column. Soon after capillary columns were first described [1] it was clear that their use enabled columns of very high theoretical plate efficiency to be operated successfully, and analyses of a given plate efficiency to be carried out much faster than had been possible with packed columns. It was therefore natural that capillary columns were considered to be faster than packed columns, but Purnell [2,3] has claimed that in certain circumstances the packed column may be faster than the capillary. His analysis is based upon the differences in the operating conditions of the two types of column and rests particularly on the difference between the experimentally important separation factor S and the theoretically important plate number N (see equations 1, 2, and 4 below). As we now show, there is little to choose between the two types of column if one evaluates the minimum analysis time consistent with certain experimental limitations.

An isothermally operated gas-chromatographic column, packed or capillary, can be regarded as a system of five degrees of freedom. The most convenient independent variables are: (1) the column length, l; (2) the column radius for a capillary or the particle radius for a packed column, r; (3) the thickness of the liquid film, d, or alternatively the ratio of film thickness to radius, $\rho = d/r$; (4) the linear gas velocity, u; (5) the solubility, α, of the substance being chromatographed or the closely related column capacity coefficient k (see equation 3).

Two other factors can be varied, but for practical reasons they cannot be regarded as truly independent variables, *viz.*, the properties of the carrier gas and of the liquid phase. They enter into the theoretical equations for the speed of analysis in the form of the diffusion coefficients D_g and D_l of substances in the gas and the liquid phase, and the viscosity η of the gas. Change of carrier gas or liquid phase alters these properties discontinuously, but changes of the column temperature and pressure alter them continuously. In practice, however, both the nature of the phases and their temperature and pressure are fixed by considerations other than the attainment of high analysis speeds. We therefore regard them as variables fixed beforehand and we take D_g, D_l, and η as constants.

The number of theoretical plates, which is the basic measure of the efficiency of any column, is denoted by N and is related to the shape of individual chromatographic peaks by any of several well-known formulæ, one of which is

$$N = 8(V_R/w_e)^2 = 8[(V'_R + v_g)/w_e]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where V_R = total retention volume from the beginning of the chromatogram; V'_R = retention volume from the " air peak," the net retention volume; v_g = gas phase volume of the column = retention volume of the " air peak "; w_e = peak breadth (in same units as V_R) at 1/2·718 of the maximum peak height.*

* All the mathematical symbols used are summarised in an appendix (p. 441).

[1] Golay, in " Gas Chromatography (Report of Symposium), 1958," ed. Desty, Butterworths, London, p. 36.
[2] Purnell, *J.*, 1960, 1268.
[3] Purnell, *Nature*, 1959, **184**, 2009.

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For the purpose of evaluating the efficiency with which a column can separate substances, a more useful quantity is the separation factor S, defined as

$$S = 8(V'_R/w_e)^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The net retention volume, rather than the total retention volume, is related directly to the solubility,

$$\begin{aligned} V'_R/v_g = k &= \alpha v_l/v_g \\ &= \alpha\beta d/r = \alpha\beta\rho \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3) \end{aligned}$$

where v_l and v_g are the volumes of the liquid and the gas phase in the column and β is a constant for any type of column. For a capillary $\beta = 2$; for a packed column $\beta = 3(1 - e)/e$ where e = the porosity of the packed column (fraction of total volume occupied by gas). Generally e is about 0·4 and $\beta \approx 4$. S and N are thus related by the equation

$$N = S[(1 + k)/k]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

For a column of length l the height of a theoretical plate (HETP) is

$$H = l/N = (l/S)[k/(1 + k)]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4a)$$

Theoretical equations for H in terms of column parameters already defined have been given by van Deempter (see Desty *et al.*[4]) for packed columns

$$H = 4\lambda r + \frac{2\gamma D_g}{u} + \left\{\frac{1}{25}\cdot\left(\frac{k}{(1+k)}\right)^2\frac{r^2}{D_g} + \frac{2}{3}\cdot\frac{k}{(1+k)^2}\cdot\frac{d^2}{D_l}\right\}u \quad . \quad . \quad (5a)$$

$$= 4\lambda r + \frac{2\gamma D_g}{u} + \left\{\frac{1}{25}\left(\frac{k}{1+k}\right)^2\frac{1}{D_g} + \frac{2}{3}\cdot\frac{k}{(1+k)^2}\cdot\frac{\rho^2}{D_l}\right\}ur^2 \quad . \quad . \quad . \quad (5b)$$

$$= A + B/u + (C_1 + C_2)u \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5c)$$

and by Golay [1] for capillary columns

$$H = \frac{2D_g}{u} + \left\{\frac{1 + 6k + 11k^2}{24(1+k)^2}\cdot\frac{r^2}{D_g} + \frac{2}{3}\frac{k}{(1+k)^2}\cdot\frac{d^2}{D_l}\right\}u \quad . \quad . \quad (6a)$$

$$= \frac{2D_g}{u} + \left\{\frac{1 + 6k + 11k^2}{26(1+k)^2}\cdot\frac{1}{D_g} + \frac{2}{3}\frac{k}{(1+k)^2}\cdot\frac{\rho^2}{D_l}\right\}ur^2 \quad . \quad . \quad (6b)$$

$$= B/u + (C_1 + C_2)u \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6c)$$

There are four terms in the equation for a packed column, and three in that for a capillary column. They are respectively the contributions of: (A) eddy diffusion due to different paths round particles in a packed column, where λ is a constant of the order of unity; this effect is absent in a capillary column; (B) longitudinal diffusion, where γ is a constant of the order of unity; (C_1) and (C_2) the slowness of transverse diffusion in the gas and the liquid phase respectively. It may be noted that the liquid transverse diffusion term is the same for both packed and capillary columns, while the gas-phase transverse diffusion term is generally greater for capillary columns.

Experimentally (A) is apparently relatively unimportant for packed columns with small particles,[5,6] and for convenience we set $A = 0$, noting that we thereby make the packed column rather more efficient than it would actually be in practice. Since we are

[4] Desty, Goldup, and Whyman, *J. Inst. Petroleum*, 1959, **45**, 287.
[5] Littlewood, in ref. 1, p. 23.
[6] Bohemen and Purnell, in ref. 1, p. 6.

interested in the separation factor rather than theoretical plate number, we replace H by the value given in equation (4*a*):

$$\text{Packed: } S^{-1} = \left(\frac{1+k}{k}\right)^2 \cdot \frac{2\gamma D_g}{ul} + \left\{\frac{1}{25D_g} + \frac{2}{3}\cdot\frac{1}{k}\cdot\frac{\rho^2}{D_l}\right\} ur^2/l \quad . \quad . \quad . \quad (7)$$

$$\text{Capillary: } S^{-1} = \left(\frac{1+k}{k}\right)^2 \cdot \frac{2D_g}{ul} + \left\{\frac{1+6k+11k^2}{24k^2D_g} + \frac{2}{3}\cdot\frac{1}{k}\cdot\frac{\rho^2}{D_l}\right\} ur^2/l \quad . \quad (8)$$

The two equations may be summarised in the form

$$S^{-1} = P/ul + Qur^2/l \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

The retention time of any substance whose column partition coefficient is k is

$$t = (1+k)l/u \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

The linear gas velocity is related to column length, the column or particle radius, and the pressure drop Δp across the column by the Poiseuille equation for a capillary tube and by the Kozeny–Carman equation [7] for a packed column. These equations are:

Poiseuille equation: $$u = \Delta p r^2/8\eta l \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

Kozeny–Carman equation: $$u = (\Delta p r^2/9\eta l)e^2/\mu(1-e)^2$$

$$= f/ae = f/a_g \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12a)$$

where μ is a constant between 4·5 and 5·0 for spheres; f = volume flow rate through column; a = total cross-sectional area of column. Direct experiment [8] shows that for randomly packed spheres the porosity lies between 0·36 and 0·42. This is confirmed by experiments described later for columns packed by the conventional gas-chromatographic procedure. With $e = 0{\cdot}38$ and $\mu = 4{\cdot}8$, equation (12*a*) becomes

$$u = \Delta p r^2/115\eta l \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12b)$$

Both equations may be summarised in the form

$$u = r^2/Dl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

The variables u and l can thus be replaced by t and D in equation (9), giving

$$S^{-1} = PD/r^2 + Q(1+k)r^2/t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

This equation involves the variables S, k, r, Δp, ρ, and t.

The time for analysis can be varied by changing any of the first five variables and can theoretically be reduced to zero. However, this possibility is not of practical importance since it involves making S zero or Δp infinite. In order to obtain a practicable value for the minimum time these two variables must be restricted. One inevitably works with an apparatus which can develop a maximum pressure drop across any column. Since any increase in Δp (*i.e.*, decrease in D) can be made to increase the speed of analysis we can, for the purpose of evaluating the maximum speed, regard Δp as being a constant.

Further, one is always interested in obtaining a given degree of separation between substances. This implies a minimum S. The separation factor required for any two substances has been evaluated by Glueckauf [9] in terms of the desired purity of the two substances and their relative solubilities in the liquid phase. The closer the solubilities and the higher the purity required the greater is the separation factor required. Purnell

[7] Carman, "Flow of Gases Through Porous Media," Butterworths Scient. Publ., 1956.
[8] Carman, *Trans. Inst. Chem. Engineers*, 1937, **15**, 150.
[9] Glueckauf, *Trans. Faraday Soc.*, 1955, **51**, 34.

has deduced that the separation factor required, when the peaks are separated by six standard deviations, is approximately

$$S = 36[(\alpha_{12}/(1 - \alpha_{12})]^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

where α_{12} is the ratio of the solubilities of the two substances.

The problem is therefore to derive the minimum time for the elution of a substance from a column with a given separation factor S and working with a pressure drop Δp. We assume, first, that k and ρ are constant and determine the optimum column radius. This is equivalent to considering the elution of a given substance from a series of columns all containing the same percentage of liquid phase. We then examine how the analysis time at the optimum column radius can be further reduced by altering k and ρ.

Differentiating equation (14) and setting $dt/dr = 0$, we have

$$-2PD/r^3 + 2Qr(1 + k)/t = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16a)$$

$$t = Q(1 + k)r^4/PD \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (16b)$$

Substituting into equation (14), we obtain

$$t = 4PDQ(1 + k)S^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (17)$$

$$r^2 = 2PDS \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (18)$$

The other parameters can then be evaluated from equations (4*a*), (10), and (13). They are given in Table 1.

The values of H and u evaluated in this way are readily shown to be those for the minimum in the well-known HETP–u curve. Equations (5) and (6) may be written in the form

$$H = 2\gamma D_g/u + [k/(1 + k)]^2 Qr^2 u \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (19)$$

$$= B/u + Cu$$

The plot of H against u is a curve with a minimum H value given by $H^2 = 4BC$ at a linear velocity given by $u^2 = B/C$; *i.e.*,

$$H^2 = 8\gamma D_g[k/(1 + k)]^2 Qr^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (20)$$

$$u^2 = 2D_g[(1 + k)/k]^2/Qr^2 = (2DSQ)^{-1} \quad . \quad . \quad . \quad . \quad . \quad (21)$$

These values are identical with those of Table 1.

TABLE 1. *Columns parameters for minimum analysis times.*

Time: $t = 8\gamma DD_g[(1 + k)^3/k^2]S^2Q$
Radius: $r^2 = 4\gamma DD_g[(1 + k)/k]^2S$
Length: $l^2 = 2r^4SQ/D$
Gas velocity: $u^2 = (2DSQ)^{-1}$
HETP: $H^2 = 8\gamma D_g[k/(1 + k)]^2Qr^2$

$D_{\text{capillary}} = 8\eta/\Delta p$	$D_{\text{packed}} = (43\eta/\Delta p)(1 - e)^2/e^2$	$e = 0{\cdot}38$
$\gamma_{\text{capillary}} = 1{\cdot}00$	$\gamma_{\text{packed}} =$ constant of order of unity	
$Q_{\text{capillary}} = \left\{\frac{1 + 6k + 11k^2}{24k^2D_g} + \frac{2}{3k}\cdot\frac{\rho^2}{D_l}\right\}$	$Q_{\text{packed}} = \left\{\frac{1}{25D_g} + \frac{2}{3k}\cdot\frac{\rho^2}{D_l}\right\}$	

If therefore one has a given Δp and requires a definite S value, and if one can choose the column radius freely, there is no possibility of obtaining a faster analysis by using a longer, wider column with intrinsically a higher S value, even if a high gas velocity is used. Only if one is limited to the available column radii or particle diameters can one hope to increase speed by using too high a gas velocity. In such a situation the column length is

decreased and the velocity increased until the separation has declined to the minimum acceptable value. In view of this, the device described by Desty [10] for winding glass capillaries of any desired radius will be a valuable aid in the experimental approach to high-speed gas chromatography.

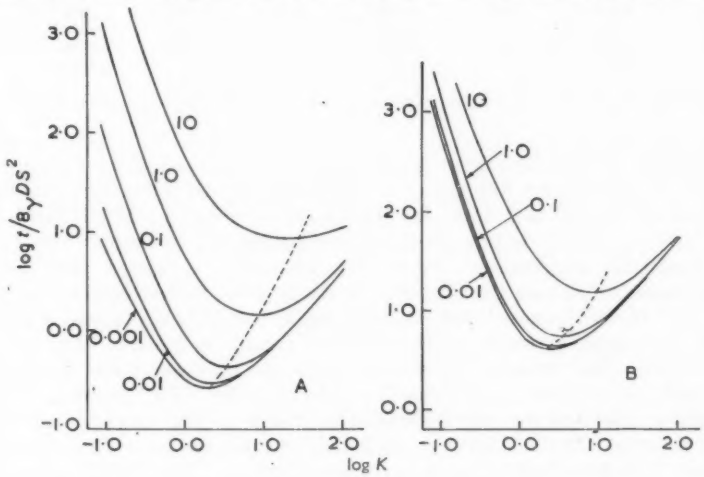
The explicit equations for the minimum time are

$$\text{Packed:} \qquad t = 8\gamma DS^2 \cdot \frac{(1+k)^3}{k^2} \cdot \left\{0{\cdot}040 + \frac{2}{3}\frac{\rho^2}{k}\frac{D_g}{D_l}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad (22)$$

$$\text{Capillary:} \qquad t = 8DS^2 \cdot \frac{(1+k)^3}{k^2} \cdot \left\{\frac{1+6k+11k^2}{24k^2} + \frac{2}{3}\frac{\rho^2}{k}\frac{D_g}{D_l}\right\} \quad . \quad . \quad . \quad (23)$$

t can always be reduced by reducing ρ, and a minimum for t is obtained at $\rho = 0$. Variation of k for $\rho = 0$ shows that the ultimate minimum occurs for a value of k close to 2 for both types of column. However, this minimum is unattainable in practice since a value of

Plots of log $(t/8\gamma DS^2)$ *against* log K *for* (A) *packed columns and* (B) *capillary columns.*



$\rho = 0$, with $k = 2$, means that the solubility α must be infinite. In order to obtain minimum times for the two types of column which have any physical significance it is necessary to consider a series of values of ρ, which are within a physically acceptable range from the point of view of the solubilities demanded. For organic vapours in hydrogen and nitrogen at atmospheric pressure, D_g takes the values of approximately 0·6 and 0·1 cm.^{2} sec.$^{-1}$. D_l for organic substances in the type of liquid used for gas chromatography is probably between 5×10^{-6} and 5×10^{-7} cm.^{2} sec.$^{-1}$. The ratio D_g/D_l is thus likely to be in the range of 10^4—10^6. In the Figures the values of $t/8\gamma DS^2$ have been plotted against k for the values of $\rho^2 D_g/D_l$ given against the individual curves. The curves have minima depending upon the value of $\rho^2 D_g/D_l$ from $k = 2$ to $k = 30$. The values of k and α for the minimum times are given in Table 2 for both types of column. One notes that the minimum values of $t/8\gamma DS^2$ for the packed column are lower than for the capillary by factors ranging from 2 for rather thick liquid films to 15 for the thinnest films. However, D is about 15 times larger for the packed column than for the

[10] Desty, *Analyt. Chem.*, 1960, **32**, 302.

capillary. The minimum analysis times are thus comparable on the two columns for very thin films but greater on the packed column for the thicker films. It should, however, be pointed out that this dependence upon relative film thickness results from the different dependence of Q upon k for the two types of column. A unified theoretical treatment of the capillary and packed columns might well eliminate this difference.

TABLE 2. *Values of k for minimum analysis times at different ρ values.*

$\text{Log}_{10}\rho$ for D_g/D_l			$\frac{t}{8\gamma DS^2}$	k	Solubility for D_g/D_l		
10^4	10^5	10^6			10^4	10^5	10^6
Capillary columns							
−1·5	−2·0	−2·5	15·3	10	160	500	1600
−2·0	−2·5 *	−3·0	5·5 *	3·3 *	165	520 *	1650
−2·5	−3·0	−3·5	4·2	2·5	400	1250	4000
−3·0	−3·5	−4·0	4·0	2·0	1000	3200	10,000
	zero		4·0	2·0		infinite	
Packed columns							
−1·5	−2·0	−2·5	8·6	30	240	740	2400
−2·0	−2·5	−3·0	1·42	9	220	710	2200
−2·5	−3·0 *	−3·5	0·46 *	4 *	320	1000 *	3200
−3·0	−3·5	−4·0	0·29	2·5	630	2000	6300
−3·5	−4·0	−4·5	0·27	2·0	1700	5300	17,000
	zero		0·27	2·0		infinite	

* Conditions chosen for evaluation of minimum practicable analysis times given in Tables 3 and 4.

The solubility of the chromatographed vapour in the liquid phase at the minimum analysis time for any relative film thickness varies only slightly when the film is thick, but begins to increase rapidly as it decreases below a value for which $\rho^2 D_g/D_l \simeq 10^{-1}$. At this point the time for analysis is only about twice the ultimate minimum. This value thus makes a reasonable compromise between the desirability of a close approach to the ultimate minimum time and the difficulty of meeting the increasingly severe solubility requirements. It may be noted that a slightly higher solubility is required with a packed column for any given approach to the ultimate minimum analysis time than with a capillary column. The difference is however slight and may well result from differences in the methods of derivation of the van Deempter and the Golay equation. The rather high solubilities required for any reasonable approach to the minimum analysis time result from the great difference between the liquid- and the gas-phase diffusion coefficients. If this difference is decreased the solubility required is less. There will therefore be some practical advantage in using nitrogen or argon as carrier gases instead of hydrogen or helium, and in using high pressures (when D_g is lower). Nitrogen, however, has a disadvantage in having a higher viscosity than hydrogen (by a factor of about 2), and since D is proportional to the viscosity one loses some analytical speed if nitrogen is used, but since viscosity does not change with pressure this disadvantage is not encountered when higher operating pressure are used. However, the slight disadvantage of using nitrogen as carrier may be far outweighed by the difficulty of obtaining a high enough solubility to make full use of the advantages of hydrogen or helium. Nevertheless, solubilities of the order of 10^2—10^3 are normal in gas chromatography [11] and there should not be any serious difficulty on this score in approaching the conditions for high speed analysis except when one is dealing with highly volatile substances. For fast analysis of these it will be necessary to work with refrigerated columns. Several liquid phases have already been successfully used by the author for columns operating at −80°.

A rough idea of the minimum practicable analysis times along with the other column dimensions may be obtained by taking values of the parameters η, D_g, D_l, ρ, and Δp. The

[11] Kwantes and Rijnders, in ref. 1, p. 125.

relevant data are given in Tables 3 and 4 for capillary and packed columns. The value of $\rho = 10^{-2.5}$ taken for the capillary column is comparable with the current experimental values and represents a 0·65% by volume coating with liquid phase. The value of $\rho = 10^{-3}$ taken for the packed column represents a coating of approximately 0·2% of the total volume of the column. When using Celite, which has a packed density of about 0·25 g./ml., this is equivalent to a 0·6% loading by weight. This is rather less than is normal in high-efficiency columns but it is not unreasonably small.

From Tables 3 and 4 it is seen that the particle radius for the packed column is some three times the radius of the equivalent capillary, whereas ρ is about three times less. The

TABLE 3. *Capillary-column parameters for minimum analysis times: nitrogen as carrier gas.*

$D_g = 0{\cdot}10$. $\eta = 2{\cdot}0 \times 10^{-4}$. $k = 3{\cdot}3$. $\alpha = 520$. $D_l = 10^{-6}$. $D = 1{\cdot}6 \times 10^{-5}$. $Q = 7{\cdot}4$. $\Delta p = 10^6$ (1 atm.).

(All quantities expressed in c.g.s. units.)

Separation factor	Time for elution (sec.)	Column diam. (mm.)	Column length (cm.)	Gas velocity (cm./sec.)
100	7×10^{-4}	0·0065	0·10	650
1000	7×10^{-2}	0·020	3·2	200
10,000	7	0·065	100	65
100,000	700	0·20	3,200	20
1,000,000	70,000	0·65	100,000	6·5
S	$7 \times 10^{-8}S^2$	$6{\cdot}5 \times 10^{-5}S^{\frac{1}{2}}$	$10^{-4}S^{\frac{1}{2}}$	$6{\cdot}5 \times 10^3 S^{-\frac{1}{2}}$

TABLE 4. *Packed-column parameters for minimum analysis times: nitrogen as carrier gas.*

$D_g = 0{\cdot}10$. $\eta = 2{\cdot}0 \times 10^{-4}$. $k = 4{\cdot}0$. $\alpha = 1000$. $\epsilon = 0{\cdot}38$. $D_l = 10^{-6}$. $\Delta p = 10^6$. $Q = 0{\cdot}57$. $D = 2{\cdot}4 \times 10^{-5}$. $\gamma = 1{\cdot}5$.

(All quantities expressed in c.g.s. units.)

Separation factor	Time for elution (sec.)	Particle diam. (mm.)	B.S.S. mesh	Column length (cm.)	Gas velocity (cm./sec.)
100	0·0013	0·03	420	0·15	600
1000	0·13	0·09	130	5·0	190
10,000	13	0·3	42	155	60
100,000	1300	0·9	13	5,000	19
1,000,000	130,000	3·0	4·2	155,000	6
S	$1{\cdot}3 \times 10^{-7}S^2$	$3{\cdot}0 \times 10^{-4}S^{\frac{1}{2}}$	12·7/(diam.)	$1{\cdot}55 \times 10^{-4}S^{\frac{1}{2}}$	$6 \times 10^3 S^{-\frac{1}{2}}$

liquid film thicknesses are thus similar. For columns giving an S value of 10^3 the film thickness will be only about 400 Å, although for an S value of 10^5 it is 4000 Å. Condon [12] has recently shown that in a working capillary column a film thickness of about 3000—4000 Å appeared quite stable and was evenly deposited. One might question whether thicknesses of less than 1000 Å could be deposited evenly, but this is till a matter for experiment. With such low liquid-phase loading it appears that normal gas-chromatographic supports such as Celite and firebrick should be replaced by more inert materials such as Nylon or glass beads. The rough porous materials which are generally used are only valuable if a high liquid-phase loading is required. They have the disadvantage that the liquid phase may well be trapped in pores which are relatively inaccessible, leading to larger values of C than would be predicted from the theoretical equation. Further, firebricks and Celite have undesirable adsorptive properties which will become increasingly noticeable as the amount of liquid phase is reduced.

It appears then that there is little to choose between the two types of column as far as practicable maximum analysis speeds are concerned. Both appear to be capable of considerably greater speeds than have so far been attained. Theory indicates that the

[12] Condon, *Analyt. Chem.*, 1959, **31**, 1717.

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packed column is likely to be somewhat slower than the capillary especially if it is remembered that the eddy diffusion term has been taken as zero throughout the treatment given above.

We are therefore free to consider which type of column is the best for any type of analysis on grounds other than speed. It is clear that the operation of a capillary column with $S = 1000$ where diameter = 0·02 mm. and $l = 3{\cdot}2$ cm. is going to be exceedingly difficult in practice because of the exceedingly small column volume and the necessity of using an incredibly small sample size and very small injection systems and detectors. With a packed column, the gas-phase volume of the column can be some 100 times greater than that of the corresponding capillary. The sample size, injection system, and detector volume can be correspondingly increased in size. Thus the packed column is certainly the most convenient for analyses requiring values of S up to about 10,000. For higher values of S the size of the packed column makes it unwieldy, and the capillary column has obvious advantages.

Experimental

The Kozeny–Carman equation [7] is known to hold well for spherical particles with the constant $\mu = 5$. The particles used in gas chromatography are not normally spherical and may therefore offer rather different resistances to flow from that predicted by the equation.

In order to test this, columns were prepared by the usual gas-chromatographic procedure containing closely screened fractions of various supports, *viz.*, Celite, firebrick (Moler Products, Colchester), and glass beads. The true porosity of the glass beads was determined by measuring their packed volume and the volume of water displaced by them. Both 60—90 and 2·5—4 mesh beads had a porosity of 0·36—0·38, in agreement with the literature values.[7]

The volume-flow rates through the columns were measured with a soap-bubble flow meter and were linearly proportional to the pressure drop across the columns for all particles studied. The results are presented in Table 5, where the equation is tested by evaluating the viscosity of the gas (oxygen) on the assumption that $\mu = 4{\cdot}8$ and $\epsilon = 0{\cdot}38$. For glass beads and firebrick the agreement between the calculated and true values of the viscosity is good, but for Celite the calculated viscosities are low, indicating that the porosity is higher than 0·38. Calculations

Table 5. *The porosity of gas-chromatographic supports.*

Gas, oxygen. Viscosity of oxygen = 2·0 × 10^{-4} poise. Porosity assumed = 0·38. $\mu = 4{\cdot}8$.

Material	Mesh B.S.S.	Particle diam. (mm.)	10^4 × Viscosity by K.–C. eqn.	Calc. porosity
Firebrick	40—43	0·310	1·59	0·40
	60—65	0·203	1·95	0·38
	90—95	0·137	1·98	0·38
	140—150	0·085	1·40	0·41
Glass spheres	60—65	0·203	1·95	0·38
Celite	60—65	0·203	1·09	0·44
	90—95	0·137	0·75	0·47
	140—150	0·085	0·65	0·49

of the porosity assuming $\mu = 4{\cdot}8$, and taking the correct viscosity for oxygen give the values in the last column of the Table. For Celite the calculated porosity increases as the particle diameter decreases. This suggests that the particles are themselves somewhat porous and that the importance of flow through the particles increases as the space between them becomes more and more constricted. For high-speed chromatography diffusion in and out of the Celite granules may become a limiting process and could reduce efficiencies below the theoretically attainable limit.

Conclusions.—(1) There should in theory be no significant difference in the ultimate speeds attainable with capillary and packed columns if they are operated under the same external experimental conditions and if the same separation number is required. (2) For the highest speed, the column of the correct dimensions has to be operated at the gas

velocity which gives the minimum HETP. (3) Hydrogen and helium can give faster analysis than nitrogen and argon if the more severe solubility requirements can be met. (4) The solubility required for maximum speed on a packed column is slightly greater than that required for a capillary column. (5) Maximum speed is obtainable with a coating of roughly 0·5% (by vol.) in a capillary and of 0·2% (by vol.) for a packed column. These represent roughly the same film thickness for equivalent columns. (6) Since such low % coatings are required, it is likely that inert packings such as glass beads, nylon, or Teflon spheres may eventually prove the best supports. Firebrick should certainly not be used for high-performance columns except for the analysis of particular mixtures which are not adsorbed by it. (7) The speed of analysis can be increased by increasing the pressure drop across the column but the average column pressure has little effect upon the speed.

Appendix: Definitions of Symbols

a, a_g, a_l	Cross-sectional areas of column, gas phase in column, and liquid phase in column.
α	Solubility: concentration of chromatographed substance in liquid phase divided by concentration in gas phase.
A, B, C_1, C_2	Generalised coefficients in plate-height equations defined in equations (5*c*) and (6*c*).
β	Constant characteristic of any type of column defined in equation (3).
γ	Constant in the van Deempter equation.
d	Average film thickness.
D	Generalised coefficient in viscosity (equation 13).
D_g, D_l	Diffusion coefficients of chromatographed substance in gas and liquid phases.
ϵ	Porosity of a packed column.
f	Volume flow rate through column.
η	Viscosity of carrier gas.
H	Height equivalent to a theoretical plate, the HETP.
k	Column capacity coefficient: amount of chromatographed substance per unit length of column in liquid phase divided by amount per unit length in gas phase.
l	Length of column.
λ	Constant in the van Deempter equation.
μ	Constant in the Kozeny–Carman equation.
N	Number of theoretical plates.
P, Q	Generalised coefficients defined in equations 7, 8, and 9.
Δp	Pressure drop across column.
r	Radius of a capillary column, or radius of particles in a packed column.
ρ	Ratio of film thickness to radius: $\rho = d/r$.
S	Separation factor defined in equation (4).
t	Elution time for any substance.
u	Linear gas velocity in column.
v_g, v_l	Volumes of gas and liquid phases in column.
V_R	Total retention volume.
V_R'	Net retention volume: $V_R' = V_R - v_g$.
w_e	Peak breadth at a height 1/2·718 of the maximum.

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78. *The Reaction of Thiourea with Dialkyl Phosphites and Trialkyl Phosphates.*

By J. B. Parker and T. D. Smith.

Treatment of thiourea with dialkyl hydrogen phosphites and trialkyl phosphates affords *N*-alkylthiouronium alkyl phosphites and *N*-alkylthiouronium dialkyl phosphates respectively. The infrared and ultraviolet spectra, electrical conductivity, and the properties of these compounds in aqueous solution have been studied.

The numerous reactions of the dialkyl phosphites show their versatility in the synthesis of organophosphorus compounds, but no previous studies of the reaction of dialkyl phosphites with thiourea have been noted. However, compounds of the general type $NRR'\cdot CX\cdot NR\cdot CH_2\cdot S\cdot PO(OR)_2$ (X = O or S) have been prepared by reaction of the appropriate urea or thiourea having an active hydrogen atom with formaldehyde and dialkyl hydrogen thiophosphate.[1]

Fig. 1. (1) *Thiourea.* (2) *Tri-n-butyl phosphate.* (3) *Reaction product of thiourea with tri-n-butyl phosphate.* (4) *Reaction product of thiourea with di-n-butyl hydrogen phosphate.*

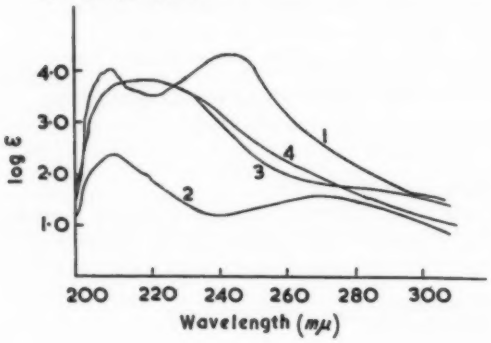
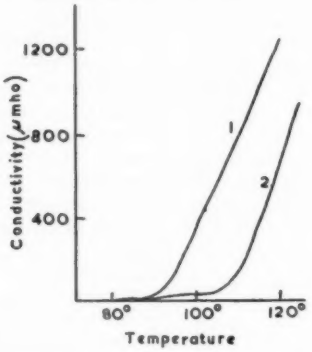


Fig. 2. *Electrical conductivity of: reaction product of thiourea* (1) *with tri-n-butyl phosphate and* (2) *with di-n-butyl hydrogen phosphite.*



Results.—A series of dialkyl hydrogen phosphites and trialkyl phosphates were mixed with thiourea in a 1 : 1 mole ratio. At room temperature no reaction took place but, on heating, the thiourea dissolved slowly to give a viscous brown oil which became dark brown above 150°. If heating was discontinued shortly after dissolution had just been effected, and the solution allowed to cool, crystalline products could be isolated in which the ratio of organic phosphorus residue to thiourea was 1 : 1. The ease of dissolution of thiourea increased on descent of homologous series and among isomers, *e.g.*, n- and iso-butyl compounds, the straight-chain compound dissolved the thiourea faster.

The solubility properties of the crystalline products varied considerably with the nature of the ester group in the parent phosphorus compound, a similar variation being noted in the carbamoyl phosphites formed by the base-catalysed reaction of dialkyl phosphites with isocyanates.[2]

Ultraviolet spectra. The ultraviolet spectra of typical compounds (in ethanol solution) are shown by Fig. 1, where the spectrum of the compound obtained from reaction of the dialkyl phosphite resembles that obtained from the trialkyl phosphate.

[1] Hook and Moss, U.S.P. 2,566,288.
[2] Fox and Venezky, *J. Amer. Chem. Soc.*, 1956, **78**, 1664.

Conductivity. A further similarity in behaviour is shown in the conductivity and change in conductivity with temperature of the solid compounds (see Fig. 2). Both compounds have a very low conductance at room temperature, which increases on melting.

Infrared spectra. From a study of the infrared absorption bands for thiourea, Quagliano *et al.*[3] made the following assignments: NH_2 bending 1617 cm.$^{-1}$, NH_2 rocking 1450 cm.$^{-1}$, N–C–N stretching 1450 cm.$^{-1}$, C=S stretching 1059 and 757 cm.$^{-1}$. From a study of the infrared spectra of a number of dialkyl phosphites and trialkyl phosphates[4,5] the following assignments have been made: P–H stretching 2435 cm.$^{-1}$, P→O stretching 1250—1300 cm.$^{-1}$, and P–O–C stretching 1030 cm.$^{-1}$ and 870 cm.$^{-1}$.

Both series of compounds obtained by reaction of thiourea with dialkyl phosphite and trialkyl phosphate were characterised by a P→O absorption at 1200—1220 cm.$^{-1}$, a lower frequency than in the parent phosphite or phosphate. The band at 2435 cm.$^{-1}$ in the spectra of the present dialkyl phosphite suffered a shift to lower frequencies. The positions of the C=S bands were close to that in thiourea itself, and the NH_2 absorption was noted at 1695 cm.$^{-1}$.

In the region 950—1100 cm.$^{-1}$ a much greater resolution was achieved in the reaction products than in the parent phosphites or phosphates, though a lower intensity of absorption was obtained for the P–O–C band at 1030 cm.$^{-1}$.

Treatment of an aqueous solution of 0·1 mole of the product obtained from the reaction of thiourea with tri-n-butyl phosphate with 0·05 mole of uranyl nitrate acidified with a few drops of dilute nitric acid gave an almost quantitative precipitation of uranyl di-n-butyl phosphate. Evaporation of the filtrate gave a residue which after recrystallisation had m. p. 56°. Analyses for carbon, hydrogen, sulphur, and nitrogen indicated the residue to be *N*-n-butylthiouronium nitrate. A similar treatment of the products obtained from the dialkyl phosphites gave a uranyl precipitate which contained the thiourea residue, no thiourea compound being obtained from the filtrate. Treatment of both products obtained from the tri-n-butyl phosphate and di-n-butyl phosphite in sodium carbonate solution with sodium nitroprusside gave a red solution immediately, and with 3,5-dinitrobenzoic acid a derivative of m. p. 168° in each case.

Discussion.—The compounds isolated from the reaction of thiourea with dialkyl phosphites and trialkyl phosphates are formed by *N*-alkylation to form *N*-alkylthiouronium alkyl phosphites and *N*-alkylthiouronium dialkyl phosphates respectively. The dialkyl phosphites have been shown to react with cacotheline in sodium carbonate solution to give an intense red coloration.[6] The *N*-alkylthiouronium alkyl phosphites give no colour since monoalkyl phosphites give no reaction with cacotheline. Treatment of thiourea with trialkyl phosphites for 5 hr. did not result in *N*-alkylation. The shifts noted in the P→O infrared absorption of the phosphate and phosphite compounds indicate considerable hydrogen bonding in these compounds and this doubtless plays an important part in the course of the reaction, allowing the possible formation of a hydrogen-bonded complex with the thiourea before alkylation takes place. Similar alkylations were attempted with urea but no reaction was noted, and use of thioacetamide instead of thiourea did not lead to *N*-alkylated products. The esters of sulphuric,[7] sulphurous,[8] and toluene-*p*-sulphonic[9] acids have been used frequently for the alkylation of amines, and Billman *et al.*[10] have described the alkylation of aromatic amines by trialkyl phosphates. In a study of the alkylation of phenols, Noller and Dutton[11] noted that alkyl borates, carbonates, nitrites, and

[3] Yamaguchi, Penland, Mizushima, Lane, Curran, and Quagliano, *J. Amer. Chem. Soc.*, 1958, **80**, 527.
[4] Meyrick and Thompson, *J.*, 1950, 225.
[5] Bellamy and Beecher, *J.*, 1953, 728.
[6] Smith, *Analyt. Chim. Acta*, 1960, **22**, 249.
[7] Claesson and Lundwall, *Ber.*, 1880, **13**, 1700.
[8] Voss and Blanke, *Annalen*, 1931, **485**, 258.
[9] Marvel and Sekera, *J. Amer. Chem. Soc.*, 1933, **55**, 345.
[10] Billman, Radike, and Mundy, *J. Amer. Chem. Soc.*, 1942, **64**, 2977.
[11] Noller and Dutton, *J. Amer. Chem. Soc.*, 1933, **55**, 424.

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phosphites were of no value though alkylation could be effected by trialkyl phosphates.

In order to assess the ability of thiourea and related compounds to undergo *N*-alkylation with other reagents and to form hydrogen-bonded compounds, thiourea was treated with dimethyl sulphoxide and dimethyl sulphite. In the former case a crystalline product was obtained, m. p. 55°, which decomposed immediately in water to give thiourea. Here alkylation did not take place and hydrogen-bonding forces alone were responsible for formation of the product. Dimethyl sulphite, on the other hand, as expected gave an analogous compound to that from trimethyl phosphate.

Experimental

The ultraviolet spectra were recorded in absolute ethanol solutions, a Unicam S.P. 500 spectrophotometer being used. The infrared spectra were recorded from Nujol mulls by use of a Perkin–Elmer Infra-cord spectrophotometer. The conductivity of the solid and fused compounds was recorded by melting the compound in a conductivity cell and allowing the melt to solidify. The conductance of the solid was then recorded at various temperatures up to the m. p., readings being made with a Wayne Kerr Universal bridge.

Reaction of Thiourea with Alkyl Phosphites and Alkyl Phosphates.—N-*n-Butylthiouronium n-butyl phosphite.* Thiourea (0·8 g.) was heated slowly with di-n-butyl phosphite (2·0 g.) to 135° and kept thereat until dissolution was complete. The temperature was then raised to 145°, and heating continued for 15 min. The mixture was cooled and extracted with hot carbon tetrachloride (3 × 50 ml.). The combined extract, on cooling, gave crude N-*n-butylthiouronium n-butyl phosphite* (1·40 g.) which, recrystallised from acetone, had m. p. 117° (Found: C, 39·2; H, 8·3; N, 9·95; S, 11·4; P, 11·9. $C_9H_{23}N_2O_3PS$ requires C, 40·0; H, 8·5; N, 10·4; S, 11·8; P, 11·9%).

N-*Alkylthiouronium salts*, NHR·CS·NH_2,HX.

	R	X	Yield (%) *	M. p.†		R	X	Yield (%) *	M. p.†
(1)	Pr^i	$Pr^iO{\cdot}PO{\cdot}OH$	39 [a]	165° [f]	(6)	Pr^n	$(Pr^nO)_2PO_2$	32 [c]	124° [g]
(2)	Et	EtO·PO(OH)	32 [a]	108 [g]	(7)	Et	$(EtO)_2PO_2$	24 [a]	145 [g]
(3)	Me	MeO·PO(OH)	34 [a]	112 [g]	(8)	Me	$(MeO)_2PO_2$	27 [d]	138 [j]
(4)	Bu^n	$(Bu^nO)_2PO_2$	33 [b]	97 [g]	(9)	Allyl	$(Allyl)_2PO_2$	40 [b]	77 [k]
(5)	Bu^i	$(Bu^iO)_2PO_2$	12 [c]	120 [h]					

	Found (%)						Required (%)				
	C	H	N	S	P	Formula	C	H	N	S	P
(1)	34·0	7·6	11·3	13·0	13·0	$C_7H_{19}N_2O_3PS$	34·7	7·85	11·6	13·2	12·8
(2)	27·8	7·0	12·8	14·5	14·9	$C_5H_{15}N_2O_3PS$	28·0	7·0	13·9	14·95	14·5
(3)	19·0	5·7	14·9	16·8	16·75	$C_3H_{11}N_2O_3PS$	19·4	5·9	15·05	17·2	16·7
(4)	44·5	8·9	8·1	9·3	9·15	$C_{13}H_{31}N_2O_4PS$	45·6	9·1	8·2	9·4	9·1
(6)	39·4	8·5	9·25	10·5	10·4	$C_{10}H_{25}N_2O_4PS$	40·0	8·3	9·3	10·7	10·3
(7)	32·0	7·3	10·6	12·2	12·1	$C_7H_{19}N_2O_4PS$	32·6	7·4	10·85	12·4	12·0
(8)	22·0	5·9	12·5	14·2	14·4	$C_4H_{11}N_2O_4PS$	22·2	6·0	13·0	14·8	14·35
(9)	40·1	6·4	9·4	10·8	10·6	$C_{10}H_{19}N_2O_4PS$	40·8	6·5	9·5	10·9	10·55

* Extracted by (*a*) hot $COMe_2$, (*b*) hot Et_2O, (*c*) cold Et_2O, (*d*) $CH_3{\cdot}CO_2Et$. † Crystallised from (*f*) $CHCl_3$, (*g*) $COMe_2$, (*h*) Et_2O–CCl_4, (*i*) $CH_3{\cdot}CO_2Et$, (*j*) H_2O–$COMe_2$, (*k*) Et_2O.

The reaction of thiourea with the other alkyl phosphites and alkyl phosphates was carried out in a similar manner, the salient features of the various syntheses being detailed in the annexed Table.

Reaction of Thiourea with Dimethyl Sulphoxide.—Thiourea (0·8 g.) was heated slowly with dimethyl sulphoxide (0·8 g.) for ½ hr. The mixture was cooled and washed with diethyl ether, and the *complex* crystallised from acetone; m. p. 55° (Found: C, 23·97; H, 6·64. $C_3H_{10}N_2OS_2$ requires C, 24·0; H, 6·7%). On treatment of the product with water, it dissociated completely, the resulting thiourea giving a precipitate immediately on addition of cupric chloride.

Reaction of Thiourea with Dimethyl Sulphite.—Thiourea (2·4 g.) was heated with dimethyl sulphite (3·30 g.) under reflux. The mixture was cooled and poured into acetone (200 c.c.); after standing, a crystalline product was obtained, which decomposed on standing. It dissolved

in water, but no precipitate was obtained when cupric chloride was added to the solution. A crystalline derivative, m. p. 225°, was obtained on treatment with 3,5-dinitrobenzoic acid.

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79. *Preparation of Monomers and Polymers containing* Sn–O–As(v) *Linkages.*

By BERTRAND L. CHAMBERLAND and ALAN G. MACDIARMID.

The compounds $[-SnMe_2\cdot O\cdot AsRO\cdot O-]_x$ (R = Me or Ph), $(SnPh_3\cdot O)_2AsPhO$, $(SnPh_3\cdot O)_3AsO$, $SnMe_3(O\cdot AsMe_2O)_2$, $[-O\cdot AsO<(O\cdot SnMe_2O)_2>AsO\cdot O\cdot SnMe_2-]_x$ and $SnMe_2(O\cdot AsPhO\cdot OH)_2$ have been prepared, three methods being involved. The properties of these products are discussed.

INTEREST has been shown recently in the preparation and properties of organometallosiloxanes, *i.e.*, compounds containing metals inserted into the –Si–O–Si–O– backbone of siloxanes. For instance, polymers and monomers of this type containing Si–O–As groups have been reported.[1] Since tin falls below silicon in Group IV of the Periodic Table and since silicon and tin(IV) have almost identical electronegativity values we have studied the preparation and properties of analogous compounds containing Sn–O–As linkages.

The only previous syntheses of such compounds involve: (*a*) interaction of alkyltin acetates with arylarsonic acids;[2] (*b*) reaction of alkyl- or aryl-tin oxides with alkyl- or arylarsonic acids;[2] and (*c*) interaction of dimethyltin dichloride with disodium arsenate.[3]

Our work involved three synthetic methods: (*a*) Reaction of the sodium or potassium salt of an arsenic-containing acid with alkyl- or aryl-tin chlorides, *viz.*:

$$x SnMe_2Cl_2 + x AsRO(ONa)_2 \longrightarrow 2x NaCl + [-SnMe_2\cdot O\cdot AsRO\cdot O-]_x \quad (1, 2)$$
(1, R = Ph; 2, R = Me)

$$2SnPh_3Cl + AsPhO(ONa)_2 \longrightarrow 2NaCl + (SnPh_3\cdot O)_2AsPhO \quad (3)$$

$$3SnPh_3Cl + 3KH_2AsO_4 \longrightarrow 3KCl + 2H_3AsO_4 + (SnPh_3\cdot O)_3AsO \quad (4)$$

(*b*) Reaction of the silver salt of an arsenic-containing acid with dimethyltin dichloride, *viz.*:

$$SnMe_2Cl_2 + 2AsMe_2O\cdot OAg \longrightarrow 2AgCl + SnMe_2(O\cdot AsMe_2O)_2 \quad (5)$$

$$3x SnMe_2Cl_2 + 2x Ag_3AsO_4 \longrightarrow 6x AgCl + [-O\cdot AsO<(O\cdot SnMe_2\cdot O)_3>AsO\cdot O\cdot SnMe_2-]_x \quad (6)$$

(*c*) Reaction of phenylarsonic acid with dimethyltin dichloride, *viz.*:

$$SnMe_2Cl_2 + 2AsPhO(OH)_2 \longrightarrow 2HCl + SnMe_2(O\cdot AsPhO\cdot OH)_2 \quad (7)$$

The same product is obtained in reaction (7) when an excess of dimethyltin dichloride is used. Only when the disodium salt of phenylarsonic acid is employed is the fully substituted derivative obtained (reaction 1).

It is of interest that the reaction analogous to (4), in which triphenylsilyl chloride[1c] was used instead of the tin compound, occurred in pure diethyl ether whereas the tin compound reacted only if a mixed aqueous solvent was used. Also, reactions analogous to (7), involving alkylsilicon halides,[1a] proceed in a non-polar solvent, but dimethyltin dichloride and phenylarsonic acid do not react in boiling benzene even in the presence of a

[1] (*a*) Kary and Frisch, *J. Amer. Chem. Soc.*, 1957, **79**, 2140; (*b*) Schmidt and Schmidbaur, *Angew. Chem.*, 1959, **71**, 553; (*c*) Chamberland and MacDiarmid, *J. Amer. Chem. Soc.*, 1960, **82**, 4542.
[2] Walde, Van Essen, jun., and Zbornik, U.S.P. 2,762,821/1956; *Chem. Abs.*, 1957, **51**, 4424.
[3] Rochow, Seyforth, and Smith, jun., *J. Amer. Chem. Soc.*, 1953, **75**, 3099.

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hydrohalogen acceptor such as pyridine, or in the molten state in the absence of solvent during 90 min. though in the presence of water a rapid reaction occurs.

Since substitution at a silicon atom, with a nucleophilic reagent, generally involves a quinquecovalent intermediate,[4] reaction of organosilicon chlorides with these arsenic compounds probably proceeds through the formation of an intermediate species of the type $\geqslant$As=O→SiCl. If the 5*d*-orbitals of tin are less effective than the 3*d*-orbitals of silicon in forming complexes of this type, then the absence of reaction of the tin compounds under similar experimental conditions is understandable. However, in the presence of a highly polar solvent, such as water, ionisation of the $\geqslant$Sn–Cl linkage will be increased and consequently a reaction mechanism involving ionisation could become more important. The experimental results strongly suggest that the reactions studied proceed by an ionisation mechanism.

The Sn–O–As linkages in the triphenyltin derivatives possess considerable covalent character as indicated by the solubility of these compounds in benzene and by their fairly low melting points. The much smaller solubility in organic solvents and absence of true melting points for the dimethyltin derivatives suggest a higher ionic character in the Sn–O–As bonds. This is to be expected since two electronegative –O–As$<$ groups attached to a tin atom will make the tin more positive—and hence the $\geqslant$Sn–O– linkages more ionic—than when only one is attached. In addition, cross-linking by $\geqslant$As=O→Sn$<$ bridges will be more favourable sterically in the dimethyltin compounds. The physical properties of the polymeric species will also be greatly affected by their degree of polymerisation.

It is evident that the Sn–O–As linkage is not extensively hydrolysed since the compounds are, in general, prepared in a medium containing large amounts of water. The solubility of certain of the compounds in aqueous acids and alkalis is probably due to the fact that in these reagents they are almost completely hydrolysed to soluble materials, *e.g.*:

$$[-O\cdot SnMe_2\cdot O\cdot AsPhO-]_x + 2xH_3O^+ \longrightarrow x[SnMe_2(H_2O)_2]^{2+} + xAsPhO(OH)_2$$
$$[-O\cdot SnMe_2\cdot O\cdot AsPhO-]_x + 2xOH^- \longrightarrow x[SnMe_2O_2]^{2-} + xAsPhO(OH)_2$$

Experimental

Infrared Spectra.—A Perkin–Elmer model 21, double-beam recording spectrophotometer with a sodium chloride prism was used. All compounds were examined in KBr discs at concentrations of approximately 2—3 mg. per 300 mg. The absorption maxima of the compounds studied are tabulated and are correlated separately for monomeric and polymeric species.

Polymeric Dimethyltin Phenylarsonate.—Addition of dimethyltin dichloride (2·20 g., 10·0 mmoles) in methanol (30 ml.) to phenylarsonic acid (2·02 g., 10·0 mmoles), which had been previously neutralised with sodium hydroxide and diluted to 60 ml. with water, yielded a white precipitate which, after washing with water and methanol and drying *in vacuo*, consisted of a pure *polymer*, $[-O\cdot SnMe_2\cdot O\cdot AsPhO-]_x$ (2·6 g., 75%), decomp. 455°, soluble in dilute acids and bases, slightly soluble in methanol and acetone, and insoluble in benzene, water, or ether (Found: C, 28·2; H, 3·3; As, 22·1. $C_8H_{11}AsO_3Sn$ requires C, 27·5; H, 3·2; As, 21·5%).

The qualitative test for $SnMe_2$ with dithizone reagent [5] was positive. In this test the deep green colour of solutions of diphenylthiocarbazone in buffered methanolic solution becomes reddish-orange on addition of a dialkyl- or triaryl-tin compound. Organoarsenic compounds do not interfere.

Polymeric Dimethyltin Methylarsonate.—Addition of dimethyltin dichloride (2·20 g., 10·0 mmoles) in water (60 ml.) to disodium methylarsonate (2·74 g., 10·0 mmoles) in water (40 ml.) yielded, after 20 min., a white gelatinous precipitate which after washing with water and methanol and drying *in vacuo* consisted of pure *polymer*, $[-O\cdot SnMe_2\cdot O\cdot AsMeO-]_x$ (1·58 g., 55%), decomp. 400°, soluble in acids and bases, slightly soluble in methanol, and insoluble in acetone,

[4] Eaborn, "Organosilicon Compounds," Butterworths Scientific Publications, London, 1960, p. 112.
[5] Aldridge and Cremer, *Analyst*, 1957, **82**, 37.

Infrared spectra ($cm.^{-1}$) *of* (*A*) $SnMe_2(O{\cdot}AsMe_2O)_2$, (*B*) $SnMe_2(O{\cdot}AsPhO{\cdot}OH)_2$, (*C*) $(SnPh_3{\cdot}O)_2AsPhO$, (*D*) $(SnPh_3{\cdot}O)_3AsO$, (*E*) $[-O{\cdot}SnMe_2{\cdot}O{\cdot}AsMeO-]_x$, (*F*) $[-O{\cdot}AsO<(O{\cdot}SnMe_2{\cdot}O)_2>AsO{\cdot}O{\cdot}SnMe_2-]_x$, and (*G*) $[-O{\cdot}SnMe_2{\cdot}O{\cdot}AsPhO-]_x$.

(*A*)	(*B*)	(*C*)	(*D*)	(*E*)	(*F*)	(*G*)
3425w	3425w	3410m	3425m	3420m	3390m	3390w
3020, 2940m	2899w	3060m	3025m	2930w	2925m	3020; 2910w
2330w	2330w	2340m				2325vw
	1980vw		1942vw			1960vw
1890; 1856vw			1888vw			1900vw
1669; 1619w	1620w	1628m	1628w			1820vw
			1576w	1629w	1628m	1620w
	1490; 1478w	1481m	1482m			1482w
1412m	1444m					1440m
		1430s	1430s		1406m	
	1310vw	1330w	1332w	1395m	1388m	
1256s						1308vw
1230w	1204w				1299m	
1175m	1158w	1178vw	1153vw	1265m		
	1092m	1091m		1184w	1190w	1180vw
		1077m	1075m		1147vw	
		1020w	1021m			1093m
	998w	997m	998m	885s		892vs
	913s			862vs	866vs	869vs
897vs	890s	885m	892s			818vs
842vs	858s	857vs	855s	756vs	766vs	762vs
	815m		832s			736m
		802s	800s			687m
	773vs		787s			
742vs	743m	723s	726vs			
	696m	693vs	693vs			
	685m	685m				

benzene, or water (Found: C, 12·9; H, 3·3; As, 26·9. $C_3H_9AsO_3Sn$ requires C, 12·6; H, 3·2; As, 26·1%). The dithizone test was positive.

Bistriphenyltin Phenylarsonate.—Addition of triphenyltin chloride (7·71 g., 20·0 mmoles) in methanol (60 ml.) to phenylarsonic acid (2·02 g., 10·0 mmoles) (previously neutralised with sodium hydroxide) in methanol (60 ml.) yielded a white precipitate which was removed by filtration after the solution had been heated to the b. p. The product obtained (7·73 g., 86%), after being washed with methanol and water and dried, melted at 245—247° and was soluble in benzene and acids, slightly soluble in acetone and methanol, and insoluble in water and bases (Found: C, 56·1; H, 4·0; As, 8·3. $C_{42}H_{35}AsO_3Sn_2$ requires C, 56·05; H, 3·9; As, 8·3%), giving a positive dithizone test.

Tristriphenyltin Arsenate.—Addition of triphenyltin chloride (3·85 g., 10·0 mmoles) in acetone (25 ml.) to potassium dihydrogen arsenate (1·80 g., 10·0 mmoles) in water (25 ml.) yielded in 48 hr. a dense oil mixed with a white solid. The mixed solvent was removed by decantation and the partly solid residue was treated with methanol to remove traces of potassium chloride and arsenic acid. In this treatment, the oil was converted into a white solid (2·34 g., 59%). This product, *tristriphenyltin arsenate*, melted at 227—230° and was soluble in benzene, slightly soluble in methanol and acetone, and insoluble in ether or water (Found: C, 54·35; H, 3·7; As, 6·6. $C_{54}H_{45}AsO_4Sn_3$ requires C, 54·5; H, 3·8; As, 6·3%), dithizone test positive.

After the above reagents had been stirred in ether at room temperature during 20 hr. they were recovered quantitatively.

Dimethyltin Cacodylate.—Addition of dimethyltin dichloride (1·10 g., 5·00 mmoles) in water (25 ml.) to silver cacodylate (2·45 g., 10·0 mmoles) in water (50 ml.) immediately precipitated silver chloride. The filtrate yielded plates of *dimethyltin cacodylate* (1·72 g., 82%) on slow evaporation. This product decomposed at 330°, was soluble in water and acids, slightly soluble in methanol, and insoluble in ether, acetone, or benzene (Found: C, 17·25; H, 4·2; As, 35·7. $C_6H_{18}As_2O_4Sn$ requires C, 17·05; H, 4·3; As, 35·45%), positive dithizone test.

Polymeric Dimethyltin Arsenate.—Addition of dimethyltin dichloride (6·60 g., 30·0 mmoles) in water (25 ml.) to silver orthoarsenate (9·56 g., 20·0 mmoles) yielded a grey precipitate. After 2 hours' refluxing and then filtration, the filtrate was evaporated to yield white flakes of pure *polymer* $[-O{\cdot}AsO<(O{\cdot}SnMe_2{\cdot}O)_2>AsO{\cdot}O{\cdot}SnMe_2-]_x$ (0·76 g.), decomp. 350°, insoluble in common

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organic solvents and only very slightly soluble in water (Found: C, 9·8; H, 2·6; As, 21·0. $C_6H_{18}As_2O_8Sn_3$ requires C, 9·95; H, 2·5; As, 20·7%), giving a positive dithizone test.

Dimethyltin Bisphenylarsonate.—Addition of phenylarsonic acid (1·01 g., 5·00 mmoles) in hot water (50 ml.) to dimethyltin dichloride (1·10 g., 5·00 mmoles), in water (25 ml.) yielded a white precipitate, which after being washed with water and dried *in vacuo*, consisted of the *bisphenylarsonate* (0·80 g., 46%), decomp. 380°, insoluble in water, acetone, ether, or benzene but dissolving in acid or base (Found: C, 30·5; H, 3·3; As, 26·9. $C_{14}H_{18}As_2O_6Sn$ requires C, 30·5; H, 3·3; As, 27·2%), giving a positive test with dithizone. The filtrate contained 99% of the chloride used, and 40% of the dimethyltin dichloride employed was recovered.

When phenylarsonic acid (4·04 g., 20·0 mmoles), in hot water (100 ml.) was added to dimethyltin dichloride (2·20 g., 10·0 mmoles) in water (25 ml.), a 73% yield was obtained (Found: C, 31·7; H, 3·4%).

Analyses were done by Galbraith Laboratories, Knoxville, Tenn.
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John Harrison Laboratory of Chemistry,
University of Pennsylvania,
Philadelphia 4, Penn., U.S.A. [*Received, June* 23*rd*, 1960.]

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80. *Phosphorylated Sugars. Part III.*[1] *The Formation of Five-, Six-, and Seven-membered Cyclic Phosphates of* 1,2-O-*Isopropylidene*-D-*glucofuranose, and the Synthesis of Two New Cyclic Phosphates of* D-*Glucose.*

By (Mrs.) Patricia Szabó and L. Szabó.

Syntheses of a seven-membered cyclic phosphate, D-glucose 3,6-(hydrogen phosphate) (VI), and of a new six-membered cyclic phosphate of D-glucose, the 3,5-(hydrogen phosphate) (XI), are described. Six- and seven-membered cyclic phosphates of 1,2-*O*-isopropylidene-D-glucofuranose and a new monophosphate of this sugar derivative have been synthesised. Cyclisation of the monophosphates of 1,2-*O*-isopropylidene-D-glucofuranose with dicyclohexylcarbodi-imide has been studied and a novel reaction of a six-membered cyclic phosphate with this reagent has been reported. Previous findings [2] on the formation of five- and six-membered cyclic phosphates and on the reactions of the former with dicyclohexylcarbodi-imide have been confirmed for the monophosphates of 1,2-*O*-isopropylidene-D-glucofuranose. Part of this work has been published in a preliminary note.[3]

In view of the importance of cyclic phosphates during the degradation of natural polyhydroxylated substances, it seemed of interest to see whether, besides the well-known five- and six-membered cyclic esters, larger phosphate-containing rings could be formed in the sugar series. Although Zeile and Kruckenberg [4] assigned a formula containing a seven-membered cyclic phosphate ring to the neutral ester which they obtained by reaction of *N*-phenylphosphoramidodichloridate with methyl α-D-glucoside, they presented no evidence to prove the structure postulated. Kenner [5] suggested that the cyclic phosphate of 7-β-D-glucopyranosyltheophylline described by Fischer [6] might be a 3,6-cyclic phosphate. For both compounds the structure of the six-membered 4,6-phosphates was later suggested [7] in view of the formation of 4,6-phosphates from both α-methyl and β-phenyl glucosides in reaction with phenyl phosphorodichloridate. The only authentic seven-membered

[1] Part II, *J.*, 1960, 3762.
[2] Khorana, Tener, Wright, and Moffatt, *J. Amer. Chem. Soc.*, 1957, **79**, 430.
[3] Szabó and Szabó, *Compt. rend.*, 1959, **249**, 1243.
[4] Zeile and Kruckenberg, *Ber.*, 1942, **75**, 1127.
[5] Kenner, *Fortschr. Chem. org. Naturstoffe*, 1951, **8**, 96.
[6] Fischer, *Ber.*, 1914, **47**, 3193.
[7] Baddiley, Buchanan, and Szabó, *J.*, 1954, 3826.

phosphorus-containing ring is the butane-1,4-diol cyclic phosphate prepared by Khorana *et al.*[2] by cyclisation of butane-1,4-diol monophosphate with dicyclohexylcarbodi-imide in aqueous pyridine. Cherbuliez and his co-workers[8] later also prepared this cyclic phosphate by treating butane-1,4-diol monophosphate with polyphosphoric acid.

1,2-*O*-Isopropylidene-D-glucofuranose 3,6-(hydrogen phosphate) (III) containing a seven-membered phosphate ring has now been prepared in three different ways, the starting material for the syntheses being in each case 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate (I). This compound was prepared by Bell[9] by nitration of 6-*O*-acetyl-1,2-*O*-isopropylidene-D-glucofuranose,[10] to give the 3,5-dinitrate, and treatment of the latter with dimethylamine. We found that good yields of 6-*O*-acetyl-1,2-*O*-isopropylidene-D-glucofuranose could not be obtained by acetylation of the glucose–boric acid complex[11] with acetic anhydride and sodium acetate.[10] The yield was much improved if the acetylation was carried out with acetic anhydride in the presence of pyridine and the product formed extracted with 1,1,2,2-tetrachloroethane instead of with chloroform. Although nitric oxides were used for nitrating the 6-acetyl-monoisopropylidene glucose in the original preparation,[9] it was here found convenient to use a modification of Honeyman and Morgan's method of nitrating sugars,[12] as described in the Experimental part. It was also found that better yields of 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate were obtained if, after the 6-acetyl-isopropylene glucose 3,5-dinitrate had reacted with dimethylamine for 48 hr. and the excess of base and the solvents had been removed,[9] the residue was taken up in benzene and the nitrated derivative exhaustively extracted into water.

1,2-*O*-Isopropylidene-D-glucofuranose 5-nitrate was phosphorylated in the first place with monophenyl phosphorodichloridate, and the resulting oily 5-nitrate 3,6-(phenyl phosphate) (II) was treated with potassium hydroxide in aqueous dioxan to remove the phenyl group. The resulting 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate 3,6-(hydrogen phosphate) (V) was isolated as its crystalline cyclohexylammonium salt.

In the second instance, 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate was phosphorylated with diphenyl phosphorochloridate, and the crystalline 6-(diphenyl phosphate) (IV) thus obtained was treated with potassium hydroxide: an excellent yield of isopropylideneglucose 5-nitrate 3,6-(hydrogen phosphate) (V) was obtained, cyclisation and loss of the phenyl group occurring simultaneously. This is in contrast to results of Khorana *et al.*[2] who found that alkaline treatment of butane-1,4-diol 4-(diphenyl phosphate) yielded tetrahydrofuran and diphenyl phosphate ion; if a similar reaction had occurred, a 3,6-anhydro-compound, in this case 3,6-anhydro-1,2-*O*-isopropylidene-D-glucose 5-nitrate, should have been formed. This compound could not, however, be detected in the reaction mixture. It is also of interest that, while 1,2-*O*-isopropylidene-3-*O*-methyl-D-glucose 6-(diphenyl phosphate) is extremely unstable,[13] yielding, by reaction of the tertiary phosphate ester with the vicinal hydroxyl group, the 5,6-(hydrogen phosphate), the monoisopropylideneglucose 5-nitrate 6-(diphenyl phosphate), which does not possess a vicinal hydroxyl group, is stable and gives a cyclic phosphate only on treatment with alkali.

When the above-mentioned oily 1,2-*O*-isopropylidene-D-glucose 5-nitrate 3,6-(phenyl phosphate) (II) was hydrogenated in the presence of Adams platinum catalyst, about three mols. of hydrogen were absorbed and the crystalline ammonium salt of 1,2-*O*-isopropylidene-D-glucofuranose 3,6-(hydrogen phosphate) (III) was obtained. The fact that the same compound was isolated when the reduction proceded in the presence of acetic acid shows that the elimination of phenol was not determined by the increase in alkalinity due to the formation of ammonia by reduction of the nitrate group.

[8] Cherbuliez, Probst, and Rabinowitz, *Helv. Chim. Acta*, 1959, **42**, 1377; 1960, **43**, 464.
[9] Bell, *J.*, 1936, 1553.
[10] Bell, *J.*, 1936, 859; Freudenberg and Hüll, *Ber.*, 1941, **74**, 237.
[11] Vargha, *Ber.*, 1933, **66**, 704.
[12] Honeyman and Morgan, *Chem. and Ind.*, 1953, 1035.
[13] Lewak, Derache, and Szabó, *Compt. rend.*, 1959, **248**, 1837.

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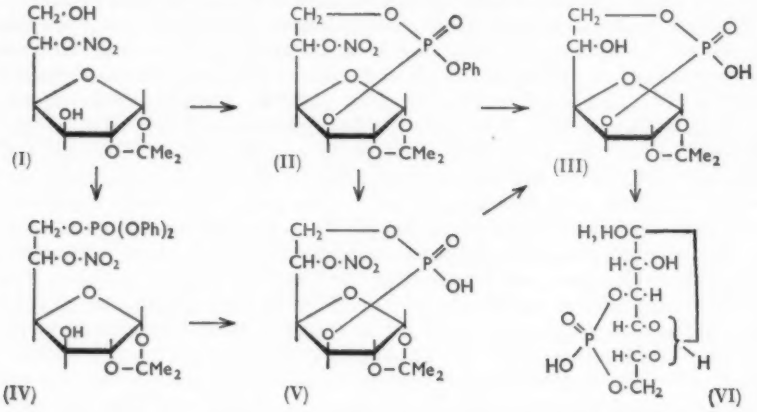
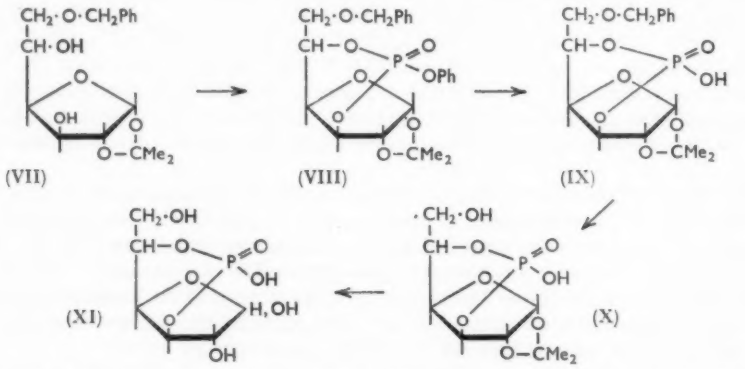
Monoisopropylideneglucose 3,6-(hydrogen phosphate) was also obtained after hydrogenation of 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate 3,6-(hydrogen phosphate) in the presence of a palladium catalyst and one equivalent of acetic acid.



The compound obtained by any of these routes was formulated as 1,2-*O*-isopropylidene-D-glucofuranose 3,6-(hydrogen phosphate) for the following reasons: electrometric titration and elementary analysis established that it was a cyclic phosphate of 1,2-*O*-isopropylidene-D-glucofuranose and it has been shown that this cyclic phosphate was neither the 3,5- nor the 5,6-cyclic phosphate, the only two other cyclic phosphates which could be formed from 1,2-*O*-isopropylidene-D-glucofuranose.

The 1,2-*O*-isopropylidene D-glucofuranose 3,5-(hydrogen phosphate) (X) mentioned above has been synthesised as follows. 6-*O*-Benzyl-1,2-*O*-isopropylidene-D-glucofuranose 3,5-(phenyl phosphate) (VIII), obtained by phosphorylation of 6-*O*-benzyl-monoisopropylideneglucofuranose [14] (VII) with monophenyl phosphorodichloridate, was treated with potassium hydroxide in aqueous dioxan to yield 6-*O*-benzyl-1,2-*O*-isopropylidene-D-glucofuranose 3,5-(hydrogen phosphate) (IX). This compound was isolated as its crystalline cyclohexylammonium salt and its structure proved by elementary analysis and



electrometric titration. It yielded 1,2-*O*-isopropylidene-D-glucofuranose 3,5-(hydrogen phosphate), also isolated as the cyclohexylammonium salt, when the benzyl group was removed by hydrogenation in the presence of a palladium catalyst.

[14] Ohle and Tessmar, *Ber.*, 1938, **71**, 1843.

The possibility that the compound formulated as the 3,6-cyclic phosphate was the 5,6-cyclic phosphate was excluded by the fact that, when the 5,6-(phenyl phosphate) resulting from the phosphorylation of 3-*O*-benzyl-1,2-*O*-isopropylidene-D-glucofuranose [15] was submitted to alkaline hydrolysis under the same conditions as were used for the hydrolyses of the 3,6- and 3,5-(phenyl phosphate), the much less stable five-membered phosphate ring was hydrolysed and after hydrogenolysis a mixture containing presumably 1,2-*O*-isopropylidene-D-glucofuranose 5- and 6-phosphates was obtained. In addition, the compound designated as the 3,6-phosphate did not react with dicyclohexylcarbodi-imide to give *N*-phosphorylureas whereas, according to Khorana and his co-workers [2] and also according to our experience, this is a general reaction of five-membered cyclic phosphates. Indeed, as will be seen below, the cyclic phosphates obtained by treatment of the 1,2-*O*-isopropylidene-D-glucofuranose 5- and 6-monophosphate underwent this reaction with the carbodi-imide.

Mild acid-hydrolysis of the 1,2-*O*-isopropylidene-D-glucofuranose 3,5- and 3,6-cyclic phosphate removed the isopropylidene groups and D-glucose 3,5- (XI) and 3,6-phosphate (VI) were isolated as their barium salts. This 3,5-cyclic phosphate is a new six-membered cyclic phosphate of D-glucose. The only other example to our knowledge is D-glucose 4,6-(hydrogen phosphate) which has been synthesised by Baddiley *et al.*[7] and which Khorana and his collaborators [2] obtained by treatment of D-glucose 6-phosphate with dicyclohexylcarbodi-imide. The 3,6-cyclic phosphate is the first example of a seven-membered cyclic phosphate of any sugar. No attempt was made to prepare the cyclohexylammonium salt of these cyclic phosphates in view of the rearrangement which readily occurred during the attempted isolation of D-glucose 4,6-(hydrogen phosphate) in this form.[7] D-Glucose 3,5- and 3,6-cyclic phosphate have different mobilities on paper chromatograms. Rapid consumption of only one equivalent of periodate by both compounds proved that the sugar was substituted on the 3-hydroxyl group. However, whereas with the 3,5-phosphate no further periodate uptake was noticed, the 3,6-phosphate slowly underwent " overoxidation," the final quantity of periodate consumed being five equivalents. This phenomenon, together with the behaviour of other sugar phosphates towards periodate, will be discussed in a future publication.

The 1,2-*O*-isopropylidene-D-glucofuranose 3,5- and 3,6-cyclic phosphate described above offered an interesting possibility of studying the cyclisation of the monophosphates of 1,2-*O*-isopropylidene-D-glucofuranose, the more so as they were easily distinguishable from each other by paper chromatography.

Khorana and his co-workers [2] have shown that, when the structure of a monophosphate is such that by cyclisation it could give theoretically either a five- or a six-membered cyclic phosphate, the formation of a five-membered ring is favoured. It is not known, however, which phosphate would be formed by the cyclisation of a monophosphate theoretically capable of giving either a six- or a seven-membered cyclic phosphate, as in the case of 1,2-*O*-isopropylidene-D-glucofuranose 3-phosphate. We therefore prepared this compound by the method of Brown, Hayes, and Todd,[16] isolating the ester as its crystalline cyclohexylammonium salt instead of its barium salt. This ester was treated with the carbodi-imide in the manner described by Khorana and his collaborators [2] and the reaction was followed by paper chromatography (for details see the Table). A cyclic phosphate having the same mobility as 1,2-*O*-isopropylidene-D-glucofuranose 3,5-cyclic phosphate was first formed. With increasing reaction time, this substance gradually disappeared and another cyclic phosphate having the same mobility as 1,2-*O*-isopropylidene-D-glucofuranose 3,6-cyclic phosphate appeared. It thus seemed that a six-membered cyclic phosphate was the first product of the reaction and that this phosphate was subsequently transformed into a seven-membered cyclic phosphate.

[15] Meyer and Reichstein, *Helv. Chim. Acta*, 1946, **29**, 152.
[16] Brown, Hayes, and Todd, *Chem. Ber.*, 1957, **90**, 936.

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Confirmation of this series of reactions was obtained by treating 1,2-*O*-isopropylidene-D-glucofuranose 3,5-cyclic phosphate with dicyclohexylcarbodi-imide under the same conditions. The 3,5-cyclic phosphate gradually disappeared and another phosphate having the same mobility as the 1,2-*O*-isopropylidene-D-glucofuranose 3,6-cyclic phosphate was formed. In addition, when 1,2-*O*-isopropylidene D-glucofuranose 3,6-(hydrogen phosphate) was treated with the carbodi-imide, no change was observed. 1,2-*O*-Isopropylidene-D-glucofuranose 3-phosphate was then treated on a larger scale with dicyclohexylcarbodi-imide and, when paper chromatography showed that the first reaction product had been completely converted into the second, the latter was isolated as its crystalline cyclohexylammonium salt. It was shown, by elementary analysis, melting point and mixed melting point, electrometric titration, and optical rotation to be 1,2-*O*-isopropylidene-D-glucofuranose 3,6-(hydrogen phosphate).

To complete this study, the cyclisation of 1,2-*O*-isopropylidene-D-glucofuranose 5- and 6-phosphate with dicyclohexylcarbodi-imide was examined.

The 5-phosphate was synthesised by phosphorylation of 3,6-di-*O*-acetyl-1,2-*O*-isopropylidene-D-glucofuranose [17] with diphenyl phosphorochloridate. The phenyl groups were removed from the crystalline diphenyl phosphate by catalytic hydrogenation, and the acetyl groups by alkaline hydrolysis, and the 1,2-*O*-isopropylidene-D-glucofuranose 5-phosphate was isolated as its crystalline monocyclohexylammonium salt.

A synthesis of 1,2-*O*-isopropylidene-D-glucofuranose 6-phosphate, isolated as its barium salt, by direct phosphorylation of 1,2-*O*-isopropylidene D-glucofuranose with phosphorus oxychloride has been described by Percival and Percival.[18] This ester has now been prepared by phosphorylation of 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-D-glucofuranose [19] with diphenyl phosphorochloridate and subsequent removal of the phenyl and benzylidene groups by hydrogenolysis; it was isolated as its crystalline dicyclohexylammonium salt.

Theoretically, two cyclic phosphates could be formed from the 5-phosphate: the five-membered 5,6-phosphate and the six-membered 3,5-phosphate. The 6-phosphate could also give two cyclic phosphates: a five-membered 5,6-phosphate, and a seven-membered 3,6-phosphate. According to Khorana and his co-workers,[2] the 5-phosphate should give the five-membered cyclic phosphate only, and this phosphate should react further with the carbodi-imide to form *N*-phosphorylureas; it is not known which phosphate would be preferred in the case of the 6-phosphate.

When the 5-phosphate was treated with dicyclohexylcarbodi-imide, a cyclic phosphate was first formed and this then reacted with more carbodi-imide to give *N*-phosphorylureas. The latter reaction, however, did not go to completion and did not therefore permit the conclusion that the 5,6-phosphate was the only cyclic phosphate formed. Moreover, it is our experience that five-membered cyclic phosphates are not quantitatively converted into *N*-phosphorylureas by this carbodi-imide. For example, when ethylene glycol cyclic phosphate (kindly presented by Dr. Jean Lecocq) was treated with the carbodi-imide in the usual conditions, *N*-phosphorylureas were formed, but considerable quantities of starting material remained even after long reaction periods (50 hr.). Thus it seems that the fact that *N*-phosphorylureas are formed proves that a five-membered cyclic phosphate is present but does not exclude the presence also of other cyclic phosphates. That only the 5,6-cyclic phosphate was formed in the reaction of the 5-phosphate with dicyclohexylcarbodi-imide was concluded from the following evidence: (1) The cyclic phosphate formed is not the 3,6-phosphate as the two compounds have different R_F values. (2) Although the cyclic phosphate formed has an R_F similar to that of the 3,5-phosphate, it cannot be the six-membered cyclic phosphate as it has been shown that the latter reacts with the carbodi-imide to give the 3,6-cyclic phosphate which was never detected during the experiments even after prolonged (53 hr.) reaction times.

[17] Freudenberg and von Oertzen, *Annalen*, 1951, **574**, 37.
[18] Percival and Percival, *J.*, 1945, 874.
[19] Brigl and Grüner, *Ber.*, 1932, **65**, 1428.

When treated with dicyclohexylcarbodi-imide, 1,2-*O*-isopropylidene-D-glucofuranose 6-phosphate behaved in the same way as the 5-phosphate. It was therefore concluded that again only the 5,6-cyclic phosphate was formed. It thus seems that a five-membered ring is formed in preference to a six- or to a seven-membered ring, and that the five-membered ring of 1,2-*O*-isopropylidene-D-glucofuranose 5,6-phosphate does not undergo transesterification analogous to that undergone by the six-membered 3,5-cyclic phosphate.

During treatment of 1,2-*O*-isopropylidene-D-glucofuranose 5-phosphate (or 6-phosphate) with the carbodi-imide, it was sometimes observed that a small amount of a substance having the same R_F as the 6-phosphate (or 5-phosphate) was formed. This observation is comparable with results of Pizer and Ballou [20] who observed the formation of some myoinositol 1-phosphate (or 2-phosphate) during the treatment of myoinositol 2-phosphate (or 1-phosphate) with dicyclohexylcarbodi-imide.

Experimental

Chloroform and ether solutions were dried over anhydrous sodium sulphate before removal of the solvent. Unless otherwise stated, evaporations were conducted under reduced pressure and specific rotations were determined for aqueous solutions.

At the end of the time specified for the phosphorylations, the solutions were cooled, a little water was added to decompose the excess of the phosphorylating agent, and the solution was left for 2 hr. before being worked up as described.

6-O-*Acetyl*-1,2-O-*isopropylidene*-D-*glucofuranose*.—Glucose (150 g.) was treated with acetone, boric acid, and concentrated sulphuric acid as described by Vargha.[11] To the crude product, isolated by removal of the unchanged acetone by distillation after neutralisation, acetic anhydride (210 ml.) and anhydrous pyridine (80 ml.) were added and the whole was heated on the water-bath. An exothermic reaction took place. It was allowed to proceed until the mixture became deep brown and was then controlled by cooling in tap-water. After remaining for 16 hr. at room temperature, the mixture was diluted with water (1·2 l.), and the aqueous solution was extracted 15 times with 1,1,2,2-tetrachloroethane (100 ml. each time). The organic phase was washed with a saturated solution of sodium hydrogen carbonate until it was neutral and then with water, dried (Na_2SO_4), and decolorised with Norite. The solvent was removed and the residue which crystallised spontaneously was recrystallised from ethyl acetate (*ca.* 150 ml.). The 6-acetate (60 g.) had m. p. 147—148° (lit.,[10] 145—146°).

6-O-*Acetyl*-1,2-O-*isopropylidene*-D-*glucofuranose* 3,5-*Dinitrate*.—A mixture of nitric acid (*d* 1·52; 16·6 ml.) and acetic anhydride (65 ml.) prepared at −40° was added to a suspension of 6-*O*-acetyl-1,2-*O*-isopropylidene-D-glucofuranose (26·2 g.) in acetic anhydride (65 ml.) cooled to −50°. The temperature was kept between −50° and −10° during the addition and until all the solids were dissolved and then between −20° and −10° for 1 hr. The solution was then cooled to −50° and chloroform (250 ml.), cooled to −50°, added. The chloroform solution was poured slowly on a solution of potassium carbonate (400 g.) in iced water (1400 ml.) containing ice (200 g.), with stirring. When the chloroform layer was neutral it was separated from the aqueous phase, washed with water, and dried. The chloroform was removed and the residue crystallised from ethanol. The 6-acetate 3,5-dinitrate (34 g., 96·5%) had m. p. 81—82° (lit.,[9] 81·5—82·5°).

1,2-O-*Isopropylidene*-D-*glucofuranose* 5-*Nitrate*.—30% Ethanolic dimethylamine (67 ml.) was added to a solution of the preceding compound (34 g.) in benzene (40 ml.), the mixture being cooled in running water during the addition. After 48 hr., the solution was evaporated to dryness below 50° under nitrogen, traces of volatile material being finally removed at 100°/0·1 mm. The crude product was dissolved in benzene and the solution exhaustively extracted with water. The combined aqueous extracts were decolorised with Norite and concentrated to a small volume. The compound which crystallised was filtered off, washed with a little water, and dried over phosphorus pentoxide. It was then dissolved in benzene (200 ml.), and the solution was concentrated on the water-bath at atmospheric pressure to 80 ml. The 5-nitrate (10 g.) which crystallised when the solution was cooled had m. p. 107·5—108° (lit.,[9] 106°).

[20] Pizer and Ballou, *J. Amer. Chem. Soc.*, 1959, **81**, 915.

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1,2-O-*Isopropylidene*-D-*glucofuranose* 5-*Nitrate* 6-(*Diphenyl Phosphate*).—Diphenyl phosphorochloridate (5·9 g.) was added slowly to a solution of 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate (5·3 g.) in anhydrous pyridine (60 ml.). The mixture was kept at 37° for 2 days. The solvents were removed and the residue was dissolved in chloroform. The chloroform solution was cooled, washed twice with ice-water, then with ice-cold sulphuric acid (1% v/v) until the aqueous layer remained acid and finally three times with ice-water, and dried. The chloroform was removed and the residue crystallised from 80% ethanol. The 6-(*diphenyl phosphate*) (7·5 g., 75%) had m. p. 116—117°, $[\alpha]_D^{23}$ +1·5° (*c* 1·28 in $CHCl_3$) (Found: C, 50·7; H, 4·7; N, 2·9; P, 6·1. $C_{21}H_{24}NO_{11}P$ requires C, 50·7; H, 4·8; N, 2·8; P, 6·2%).

1,2-O-*Isopropylidene*-D-*glucofuranose* 5-*Nitrate* 3,6-(*Hydrogen Phosphate*).—(*a*) Phenyl phosphorodichloridate (3·8 g.) in pyridine (10 ml.) was added to 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate (4·75 g.) in pyridine (40 ml.). The solution was kept at 37° for 48 hr. The pyridine was removed, the residue dissolved in chloroform, and the solution washed with water and dried. The chloroform was removed, and the residual oily 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate 3,6-(phenyl phosphate) (6·1 g.) dissolved in dioxan (87 ml.), and 2N-potassium hydroxide (8·7 ml.) added. The mixture was shaken until the oil which separated had dissolved. After 16 hr., the solution was neutralised with Amberlite IR-120 resin (H^+ form). The resin was filtered off and washed with water, and the combined filtrate and washings were concentrated to dryness. The residue was dissolved in water and the aqueous solution extracted three times with ether before being passed slowly through a column of Amberlite IR-120 (cyclohexylammonium form). The effluent was concentrated to dryness and the residue crystallised from 95% ethanol, to give 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate 3,6-(cyclohexylammonium phosphate) (3·0 g., 46·5%), m. p. 197—205° (decomp.), $[\alpha]_D^{24}$ +22° (*c* 1·08) (Found: C, 42·3; H, 6·3; N, 6·5. Calc. for $C_{18}H_{37}N_3O_{10}P$: C, 42·25; H, 6·3; N, 6·6%).

(*b*) 2N-Potassium hydroxide (15 ml.) was added to a solution of 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate 6-(diphenyl phosphate) (4·97 g.) in dioxan (50 ml.). The oil which was precipitated redissolved after the mixture had been shaken for 15 min., giving a slightly yellow solution which was kept for 16 hr. at room temperature. The solution was neutralised with Amberlite IR-120 (H^+ form) and, after removal of the resin, diluted with water and extracted three times with ether. The aqueous solution was then passed very slowly through an Amberlite IR-120 column (cyclohexylammonium form), and the effluent was concentrated. The crystalline residue was triturated with absolute ethanol, filtered off, and recrystallised from 95% ethanol. The 5-nitrate 3,6-(cyclohexylammonium phosphate) had m. p. 197—205° (decomp.), $[\alpha]_D^{24}$ +22° (*c* 1·08) (Found: C, 42·3; H, 6·3; N, 6·55%).

1,2-O-*Isopropylidene*-D-*glucofuranose* 3,6-(*Hydrogen Phosphate*).—(*a*) The oily 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate 3,6-(phenyl phosphate) obtained by phosphorylation of 1,2-*O*-isopropylidene-D-glucofuranose 5-nitrate (4·8 g.) (see above) was hydrogenated in ethanol (20 ml.) in the presence of Adams platinum. When the hydrogen uptake had ceased, the catalyst was filtered off and the solution concentrated. When triturated with ether, the residue crystallised. After recrystallisation from ethanol–ether, the ammonium salt (2·1 g., 39%) of the cyclic phosphate had m. p. 160—170° (decomp.), $[\alpha]_D^{25}$ +16·2° (*c* 0·83) (Found: C, 36·3; H, 6·0; N, 4·6. Calc. for $C_9H_{18}NO_8P$: C, 36·1; H, 6·0; N, 4·7%).

(*b*) 1,2-*O*-Isopropylidene-D-glucofuranose 5-nitrate 3,6-(cyclohexylammonium phosphate) (1·9 g.) was hydrogenated in water (50 ml.) containing acetic acid (0·24 ml.) in the presence of a palladium catalyst. When the hydrogen uptake had ceased, the catalyst was filtered off and the solution concentrated. After crystallisation from ethanol–ether, the cyclohexylammonium salt (1·4 g., 89·5%) had m. p. 195—200° (decomp.), $[\alpha]_D^{24}$ +13·6° (*c* 0·62) (Found: C, 47·1; H, 7·2; N, 3·8. Calc. for $C_{15}H_{28}NO_8P$: C, 47·2; H, 7·3; N, 3·7%).

(*c*) 1,2-*O*-Isopropylidene-D-glucofuranose 3-(dicyclohexylammonium phosphate) (1 g.) was dissolved in water (5 ml.) and transformed into the free acid by addition of an excess of Amberlite IR-120 resin (H^+ form). The resin was filtered off, and the solution neutralised with pyridine and evaporated to dryness. The residue was dissolved in water (5 ml.) containing pyridine (10 ml.), and dicyclohexylcarbodi-imide (3 g.) in pyridine (10 ml.) was added. The mixture was shaken at room temperature for 66 hr., then diluted with water (50 ml.), and the dicyclohexylurea filtered off. The aqueous solution was washed three times with ether, acidified with an excess of Amberlite IR-120 (H^+ form), filtered, and neutralised with cyclohexylamine. The solution was evaporated, the last traces of water being removed by repeated distillation with ethanol. The residue was dissolved in ethanol, and ether added to slight turbidity. The

cyclohexylammonium salt of the 3,6-(hydrogen phosphate) which crystallised had m. p. 195—200° (decomp.), $[\alpha]_D^{25}$ +13·4° (*c* 0·82) (Found: C, 47·2; H, 7·2; N, 3·7; P, 8·6. Calc. for $C_{15}H_{28}NO_8P$: C, 47·2; H, 7·3; N, 3·7; P, 8·1%).

D-*Glucose* 3,6-(*Hydrogen Phosphate*).—The ammonium salt (5·5 g.) or the cyclohexylammonium salt (7·0 g.) of 1,2-*O*-isopropylidene-D-glucofuranose 3,6-(hydrogen phosphate) was dissolved in water (75 ml.) and passed through a column of Amberlite IR-120 resin (H^+ form) (*ca.* 100 ml.), and the column was washed with water. The effluent (200 ml.) was heated in a boiling-water bath for 15 min., cooled, neutralised with 0·3N-barium hydroxide, and concentrated to 12 ml. Addition of ethanol precipitated an oil which crystallised on trituration. The *barium salt* (3·7 g., 58%) of the 3,6-cyclic phosphate recrystallised from water and ethanol and had $[\alpha]_D^{21}$ +25·5° (*c* 2·0) (Found: C, 21·0; H, 4·1. $C_6H_{10}O_8PBa_1,2H_2O$ requires C, 20·8; H, 4·05%).

6-O-*Benzyl*-1,2-O-*isopropylidene*-D-*glucofuranose* 3,5-(*Hydrogen Phosphate*).—Phenyl phosphorodichloridate (2·11 g.) was added to 6-*O*-benzyl-1,2-*O*-isopropylidene-D-glucofuranose [14] (3·1 g.), dissolved in pyridine (35 ml.). The solution was left overnight at 37°. The pyridine was removed and the residue dissolved in ether. The ether solution was washed twice with iced water, then with ice-cold (1% v/v) sulphuric acid until the aqueous phase remained acid, and finally three times with iced water, and dried. The ether was removed, the residue (3·8 g.) dissolved in dioxan (50 ml.), and 2N-potassium hydroxide (6·5 ml.) added. The mixture was shaken and after 0·5 hr. the oil which at first separated dissolved. After 16 hr., the solution was neutralised with Amberlite IR-120 resin (H^+ form). The resin was filtered off and washed with water. The combined filtrate and washings were concentrated to dryness and the residue was dissolved in water. The solution was extracted twice with ether before being passed slowly through a column of Amberlite IR-120 resin (cyclohexylammonium form). The effluent was concentrated to dryness and the residue triturated with ether until it crystallised. After recrystallisation from ethanol–ether, 6-*O*-benzyl-1,2-*O*-isopropylidene-D-glucofuranose 3,5-(cyclohexylammonium phosphate) (2·4 g., 50·9%) had m. p. 185—200° (decomp.), $[\alpha]_D^{26}$ +18·7° (*c* 0·48) (Found: C, 55·85; H, 7·2; N, 3·1. Calc. for $C_{22}H_{34}NO_8P$: C, 56·05; H, 7·2; N, 3·0%).

1,2-O-*Isopropylidene*-D-*glucofuranose* 3,5-(*Hydrogen Phosphate*).—The preceding compound (1 g.) was hydrogenated in ethanol (30 ml.) in the presence of a palladium catalyst. This gave crystals which, recrystallised from ethanol–ether, afforded the cyclohexylammonium salt (0·6 g., 75%), m. p. 180—190° (decomp.), $[\alpha]_D^{24}$ +32·0° (*c* 1·14), of the cyclic phosphate (Found: C, 47·5; H, 7·3; N, 3·75. Calc. for $C_{15}H_{28}NO_8P$: C, 47·2; H, 7·3; N, 3·7%).

D-*Glucose* 3,5-(*Hydrogen Phosphate*).—The preceding cyclohexylammonium salt (7·5 g.) was dissolved in water (75 ml.) and passed through a column of Amberlite IR-120 resin (H^+ form) (100 ml.). The effluent and washings (200 ml.) were heated on a boiling-water bath for 15 min., cooled, and neutralised with barium hydroxide solution. The aqueous solution was concentrated to dryness and the residue dissolved in the minimum amount of water. Addition of ethanol precipitated the *barium salt* (3·9 g., 60·5%) of D-glucose 3,5-phosphate. It had $[\alpha]_D^{21}$ +20·7° (*c* 2·0) (Found: C, 22·2; H, 3·8. $C_6H_{10}O_8PBa_1,H_2O$ requires C, 21·95; H, 3·7%).

3-O-*Benzyl*-1,2-O-*isopropylidene*-D-*glucofuranose* 5,6-(*Phenyl Phosphate*).—Phenyl phosphorodichloridate (3·4 g.) was added to 3-*O*-benzyl-1,2-*O*-isopropylidene-D-glucofuranose [15] (5·0 g.) in pyridine (60 ml.). The solution was kept at 37° for 48 hr. No water was added at the end of the reaction time. The pyridine was removed and the residue dissolved in cold chloroform (−15°). The chloroform layer was washed rapidly three times with ice-water and dried. After removal of the chloroform, an oily, neutral ester (6·9 g.) remained. This ester was extremely unstable. In the presence of pyridine and water, a pronounced odour of phenol developed. After treatment with potassium hydroxide (1 g. in 5 ml. of water) in dioxan (80 ml.), followed by the usual working up and hydrogenation in the presence of palladium to remove the benzyl group, the substance gave two phosphorus-containing spots on a paper chromatogram. The R_F's of these spots corresponded to those of 1,2-*O*-isopropylideneglucose 5- and 6-phosphate.

1,2-O-*Isopropylidene*-D-*glucofuranose* 3-(*Dihydrogen Phosphate*).—This ester was prepared by the method of Brown, Hayes, and Todd [16] and isolated as its dicyclohexylammonium salt which was crystallised by adding acetone to an aqueous solution of the salt. It had m. p. 155—170° (decomp.), $[\alpha]_D^{24}$ +5·5° (*c* 1·8) (Found: C, 50·5; H, 8·7; N, 5·5; P, 6·1. Calc. for $C_{21}H_{43}N_2O_9P$: C, 50·6; H, 8·6; N, 5·6; P, 6·2%).

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3,6-*Di*-O-*acetyl*-1,2-O-*isopropylidene*-D-*glucofuranose* 5-(*Diphenyl Phosphate*).—Diphenyl phosphorochloridate (4·28 g.) was added slowly to a solution of 3,6-di-*O*-acetyl-1,2-*O*-isopropylidene-D-glucofuranose [17] (4·4 g.) in anhydrous pyridine (60 ml.). The solution was kept at 37° for 48 hr. The pyridine was removed below 40° and the oily residue triturated with several lots of iced water until it crystallised. After recrystallisation from ethanol, the diphenyl phosphate (5 g., 64·5%) had m. p. 94—95°, $[\alpha]_D^{22}$ −16·9° (*c* 0·53 in $CHCl_3$) (Found: C, 56·0; H, 5·4; P, 5·7. Calc. for $C_{25}H_{29}O_{11}P$: C, 56·0; H, 5·4; P, 5·8%).

1,2-O-*Isopropylidene*-D-*glucofuranose* 5-(*Dihydrogen Phosphate*).—The above diphenyl phosphate (5 g.) was hydrogenated in absolute ethanol (200 ml.) in the presence of Adams platinum. When the hydrogen uptake ceased, the catalyst was filtered off and the solution was saturated several times with ammonia. When a paper chromatogram showed that the removal of the acetyl groups was complete, the ammonia and ethanol were removed and the residue was dissolved in water. The aqueous solution was passed slowly through a column of Amberlite IR-120 resin (cyclohexylammonium form), and the effluent concentrated. The residue was dissolved in the minimum amount of water. The monocyclohexylammonium salt of the 5-phosphate which crystallised on the addition of acetone had m. p. 170—172° (decomp.), $[\alpha]_D^{24}$ +8·4° (*c* 1·3) (Found: C, 44·0; H, 7·7; N, 3·9. Calc. for $C_{15}H_{30}NO_9P,\frac{1}{2}H_2O$: C, 44·1; H, 7·6; N, 3·4%).

1,2-O-*Isopropylidene*-D-*glucofuranose* 6-(*Dihydrogen Phosphate*).—Diphenyl phosphorochloridate (9·5 g.) was added slowly to 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-D-glucofuranose [19]

Reaction of the monophosphates of 1,2-O-*isopropylidene*-D-*glucofuranose with dicyclohexylcarbodi-imide* (DCC).

Phosphate of 1,2-*O*-isopropylidene-D-glucofuranose	R_F in Solvent A			
3-Phosphate + DCC (1 hr.)	0·42+	0·72+	0·76++	
(5 hr.)	—	0·73++	0·77++	
(22 hr.)	—	0·73++	0·77+	
(27 hr.)	—	0·73+++	—	
3,5-Phosphate + DCC (4 hr.)	—	0·72+	0·77++	
(29 hr.)		0·72+++	0·77+/−	
3-Phosphate	0·42			
3,5-Phosphate			0·77	
3,6-Phosphate		0·72		
5-Phosphate + DCC (1 hr.)	0·38+	0·49++	0·78+++	—
(7 hr.)	—	—	0·78+++	0·99+
(53 hr.)	—	—	0·78+++	0·99+
6-Phosphate + DCC (1 hr.)	0·38+	0·49+/−	0·78++	—
(7 hr.)	—	—	0·78++	0·99+
(53 hr.)	—	—	0·78++	0·99+
5-Phosphate		0·49		
6-Phosphate	0·38			
3,5-Phosphate			0·77	
3,6-Phosphate		0·72		

Phosphate of 1,2-*O*-isopropylidene-D-glucofuranose	R_F in Solvent B			
3-Phosphate + DCC (1 hr.)				
(5 hr.)	—	0·59++	0·67++	
(22 hr.)	—	0·59++	0·67+	
(27 hr.)				
3,5-Phosphate + DCC (4 hr.)		0·59+	0·67++	
(29 hr.)		0·59+++	0·67+/−	
3-Phosphate	0·16			
3,5-Phosphate			0·67	
3,6-Phosphate		0·60		
5-Phosphate + DCC (1 hr.)	0·11+	0·20++	0·57+++	0·98+
(7 hr.)	—	—	0·57+++	0·98+
(53 hr.)	—	—	0·57+++	0·98+
6-Phosphate + DCC (1 hr.)	0·11+	0·20+/−	0·58++	—
(7 hr.)	—	—	0·58++	0·98+
(53 hr.)	—	—	0·58++	0·98+
5-Phosphate		0·20		
6-Phosphate	0·11			
3,5-Phosphate			0·60	
3,6-Phosphate		0·53		

(10 g.) dissolved in anhydrous pyridine (20 ml.). The solution was kept at 37° for 48 hr. The pyridine was removed below 40° and the residue dissolved in chloroform. The chloroform solution was washed twice with iced water, then with ice-cold (1% v/v) sulphuric acid until the aqueous layer remained acid, and finally three times with iced water, and dried. The chloroform was removed and the residue hydrogenated in ethanol (200 ml.) in the presence of Adams platinum. The quantity of hydrogen absorbed corresponded to the quantity calculated for the hydrogenolysis of the two phenyl groups and of the benzylidene group. When the hydrogen uptake had ceased, the catalyst was filtered off and the solution neutralised with cyclohexylamine. The solution was concentrated to a small volume and ether was added to turbidity. The cyclohexylammonium salt (8·3 g., 51·2%) of 1,2-*O*-isopropylidene-D-glucofuranose 6-phosphate which crystallised overnight at 0° had, after one recrystallisation from water–acetone, m. p. 135—140° [resolidifies and remelts at 195—197° (decomp.)], $[\alpha]_D^{25}$ −6·9° (*c* 2·01) (Found: C, 50·5; H, 8·9; N, 5·6; P, 6·2. Calc. for $C_{21}H_{43}N_2O_9P$: C, 50·6; H, 8·6; N, 5·6; P, 6·2%).

Cyclisation of the Phosphates of 1,2-O-*Isopropylidene-*D*-glucofuranose with Dicyclohexylcarbodi-imide.*—The cyclohexylammonium salts of the monophosphates (20 mg.) were dissolved in water, and the solution was acidified with Amberlite IR-120 (H^+ form). The resin was filtered off and washed with water, and the combined filtrates were neutralised with pyridine and evaporated to dryness. The residues were dissolved in pyridine (0·8 ml.) containing water (0·2 ml.), and dicyclohexylcarbodi-imide (60 mg.) was added to the solutions which were shaken mechanically. At intervals, samples (0·2 ml.) of the solutions were removed and diluted with water (0·2 ml.), and the aqueous layer extracted three times with ether before being chromatographed. The solvent systems employed were: A, propan-2-ol–ammonia–water (7 : 1 : 2); B, propan-2-ol–ammonia–water (8 : 1 : 1). . Ascending chromatograms were run on Whatman No. 1 paper without time- or temperature-control, appropriate control substances being chromatographed at the same time. The results are given in the Table.

The authors thank Professor E. LeBreton for her interest and encouragement. They are also indebted to Mr. T. Clim for technical assistance and many large-scale preparations.

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81. *Addition Reactions of Heterocyclic Compounds. Part VIII.* Methyl Pyrrole-1-carboxylate and Dimethyl Acetylenedicarboxylate.*

By R. M. Acheson and J. M. Vernon.

Methyl pyrrole-1-carboxylate with dimethyl acetylenedicarboxylate gave acetylene and trimethyl pyrrole-1,3,4-tricarboxylate, which was degraded to dimethyl pyrrole-3,4-dicarboxylate.

The presence of an alkoxycarbonyl substituent at position 1 of the pyrrole nucleus inhibits the conjugation of the nitrogen p_π-electron pair with the π electrons of the double bonds of the ring. This reduces the susceptibility of the other ring positions to electrophilic attack. Ethyl pyrrole-1-carboxylate does not react with 2,4,6-trinitrobenzenediazonium sulphate, although many other pyrroles, including some pyrrole-2- and -3-carboxylic esters, are substituted by the less reactive *p*-nitrobenzenediazonium cation.[1]

The withdrawal of the π electrons from nitrogen by the alkoxycarbonyl group increases the aliphatic character of the ring diene system. Thus ethyl pyrrole-1-carboxylate is hydrogenated very much more easily than pyrrole itself,[2] and the hydrogenation of pyrrole

* Part VII, *Proc. Chem. Soc.*, 1960, 281.

[1] Treibs and Fritz, *Annalen*, 1958, **611**, 162.

[2] Signaigo and Adkins, *J. Amer. Chem. Soc.*, 1936, **58**, 709.

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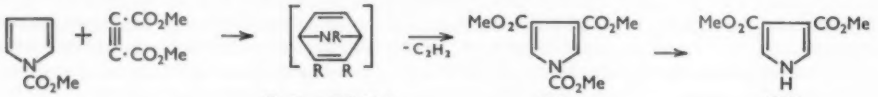
is facilitated by acids.[3] In view of this it seemed interesting to discover whether 1-alkoxycarbonylpyrroles displayed any reactivity to dienophiles, especially since no Diels–Alder addition to such systems has been attempted.

When equimolecular proportions of methyl pyrrole-1-carboxylate and dimethyl acetylenedicarboxylate were allowed to react at room temperature a yellow colour developed, but evaporation gave only a tar smelling strongly of the acetylenic ester. When dimethyl acetylenedicarboxylate was added to this pyrrole at its boiling point there was an obvious darkening and a rise in temperature. Acetylene was evolved, and the tarry product afforded chromatographically a colourless substance, $C_{10}H_{11}NO_6$, containing three methoxyl groups.

This compound is trimethyl pyrrole-1,3,4-tricarboxylate (II) and is probably formed by elimination of acetylene from the hypothetical adduct (I); attempts to isolate this intermediate after reaction at intermediate temperatures in boiling benzene or xylene gave only tars. An adduct corresponding to (I) has been obtained from 1-benzylpyrrole and acetylenedicarboxylic acid; its dihydro-derivative decomposes to ethylene and 1-benzylpyrrole-3,4-dicarboxylic acid in hot aqueous sodium carbonate.[4]



(I; R = CO_2Me) (II) (III)

Degradative evidence supporting structure (II) has been obtained. Saponification followed by acidification precipitated a potassium salt of a carboxylic acid, which gave a dimethyl ester (III), $C_8H_9NO_4$. The same dimethyl ester was obtained directly by treatment of the triester (II) with cold methanolic alkali. It gave a positive Ehrlich reaction on heating, and its melting point agreed with that reported for dimethyl pyrrole-3,4-dicarboxylate.[5] The ultraviolet absorption spectrum of the triester (II) in methanol ($\lambda_{max.}$ 2500 Å; ε 7200) resembled the spectra of other pyrrolecarboxylic esters.[6] The degradation product (III) had a similar ultraviolet absorption spectrum, with a single maximum at 2500 Å; diethyl pyrrole-3,4-dicarboxylate has an absorption maximum at 2500 Å.[6]

Experimental

Methyl Pyrrole-1-carboxylate.—Freshly distilled pyrrole (27 g.) was converted into the potassium derivative by the method of Clemo and Ramage,[7] with potassium (16 g.). Methyl chloroformate (37 g.) in ether was added dropwise to the potassiopyrrole suspended in absolute ether (200 ml.), and cooled in water. After 30 min. at room temperature, the mixture was filtered. The filtrate and ethereal washings on distillation gave *methyl pyrrole-1-carboxylate* (43 g., 84%), b. p. 168—170° (Found: C, 57·2; H, 5·5; N, 11·1. $C_6H_7NO_2$ requires C, 57·6; H, 5·6; N, 11·2%). This ester with aqueous ammonia (*d* 0·880) at 100° gave, in 3 hr., pyrrole-1-carboxyamide, plates, m. p. 163° (lit.,[8] 166°).

Trimethyl Pyrrole-1,3,4-tricarboxylate (II).—Dimethyl acetylenedicarboxylate (14·2 g.) was added gradually to methyl pyrrole-1-carboxylate (12·5 g.) at its b. p. (170°). The internal temperature rose to 200°, where it was held for 1 hr. A slow stream of dry nitrogen admitted above the vapours condensing in the reflux condenser during this time swept out copious quantities of acetylene, which were absorbed in ammoniacal cuprous chloride solution, with precipitation of cuprous acetylide. When the mixture was left overnight, crystals appeared admixed with tar. This mixture, in a little benzene, was chromatographed on a 50 cm. alumina

[3] Treibs and Kolm, *Annalen*, 1957, **606**, 166.
[4] Mandell and Blanchard, *J. Amer. Chem. Soc.*, 1957, **79**, 6198.
[5] Nicolaus and Mangoni, *Gazzetta*, 1956, **86**, 358.
[6] Scrocco and Nicolaus, *Atti Acad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1957, **22**, 500.
[7] Clemo and Ramage, *J.*, 1931, 49.
[8] Tschelinzeff and Maxoroff, *Ber.*, 1927, **60**, 194.

column (Spence grade H; deactivated with 5% of its weight of 10% aqueous acetic acid) prepared in light petroleum (b. p. 40—60°). Elution with light petroleum–benzene (1 : 1) gave the *triester* (10 g., 40%). Three recrystallisations from methanol afforded colourless crystals, m. p. 69° (Found: C, 49·9; H, 4·7; N, 6·0; OMe, 38·1%; *M*, 245. $C_{10}H_{11}NO_6$ requires C, 49·8; H, 4·6; N, 5·8; 3OMe, 38·6%; *M*, 241). In paraffin paste this showed maxima at 5·65, 5·70, and 5·80 μ in the carbonyl region.

Dimethyl Pyrrole-3,4-dicarboxylate (III).—(i) Potassium hydroxide (0·5 g.) in methanol (10 ml.) was added to trimethyl pyrrole-1,3,4-tricarboxylate (1·0 g.) in methanol (10 ml.). After 4 hr. with occasional shaking the precipitate was collected (0·7 g., 92%). Recrystallisation from a large volume of xylene gave the diester as needles, m. p. 244°.

(ii) Trimethyl pyrrole-1,3,4-tricarboxylate (1·0 g.) was heated under reflux with potassium hydroxide (1·5 g.) in methanol (10 ml.). After 24 hr. the solvent was evaporated, and the residue dissolved in water. Addition of concentrated hydrochloric acid caused effervescence, and precipitation of a colourless solid (0·5 g.), which was collected, washed, and dried. This product was infusible; it charred and left a residue when strongly heated. The product (0·3 g.) was dissolved in absolute methanol (50 ml.), saturated with dry hydrogen chloride, and left for 6 hr. The solution was evaporated to dryness and the solid residue (0·2 g.) was washed with aqueous sodium hydrogen carbonate and water, and dried. It recrystallised from methanol, giving the diester (III) as colourless prisms, m. p. 245° (lit.,[5] 245—246°; mixed with the product of the previous experiment, m. p. 244°) (Found: C, 52·8; H, 5·2; N, 7·6. Calc. for $C_8H_9NO_4$: C, 52·5; H, 5·0; N, 7·7%). In paraffin paste this showed one maximum, at 5·80 μ, in the carbonyl region, and N–H absorption at 3·10 μ.

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82. *Syntheses of Some Polymeric Polypeptides of Lanthionine.*

By Max Frankel and David Gertner.

Polymers of lanthionine having defined structure were obtained on polymerisation of suitable protected monomers, *e.g.*, the *N*-carboxy-anhydride of mono-*N*-benzyloxycarbonyl-lanthionine monobenzyl ester.

Lanthionine, a tetrafunctional diamino-dicarboxylic acid, containing a sulphur bridge between two alanine residues, was obtained from various proteins,[1] and in hydrolysates of wool or hair treated with alkali.[2] Its formation in the degradation of cystine has been discussed by Schoeberl and others.[3]

Work on polymeric peptides obtained from tetrafunctional amino-acids has been scanty. A polymeric polypeptide from cystine was obtained by Jones and Lundgren [4] from its *NN'*-dicarboxy-anhydride, but as no precautions were taken to assure linear polymerisation it might have been three-dimensional.

Our preliminary experiments were on polymerisation of suitable protected monomeric derivatives of the more accessible cystine; the known conversion of cystine by alkali into lanthionine was tried to arrive at polylanthionine derivatives.

Monobenzyloxycarbonyl-L-cystine [5] in suspension in dioxan was treated with carbonyl chloride, giving the corresponding mono-*N*-carboxy-anhydride which polymerised when heated *in vacuo*. The structure of this polymer containing the free carboxyl group may

[1] Stein, *Chem. and Ind.*, 1955, 774; Berridge, Newton, and Abraham, *Biochem. J.*, 1952, **52**, 529; Alderton and Fevold, *J. Amer. Chem. Soc.*, 1951, **73**, 463.
[2] Horn, Jones, and Ringel, *J. Biol. Chem.*, 1941, **138**, 141; 1942, **144**, 93.
[3] Schoeberl and Wagner, *Z. physiol. Chem.*, 1956, **304**, 97.
[4] Jones and Lundgren, *J. Amer. Chem. Soc.*, 1951, **73**, 5465.
[5] Marshall, Winitz, Birnbaum, and Greenstein, *J. Amer. Chem. Soc.*, 1957, **79**, 4538.

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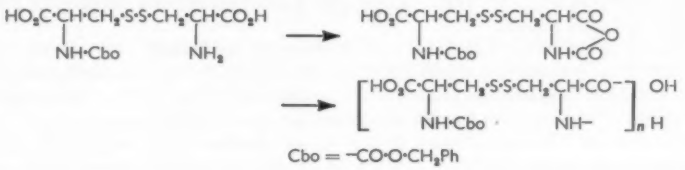
be assumed to be more defined than that obtained from the *NN'*-dicarboxy-anhydride by Jones and Lundgren.[4] Free polycystine was obtained by removal of the *N*-benzyloxycarbonyl group by hydrobromic acid in acetic acid.



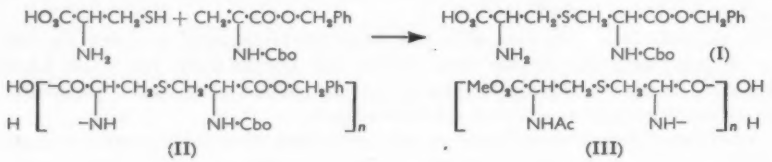
Attempts were made to obtain polylanthionine by treating the above polymer and the free polycystine with alkali, but the conversion was unsatisfactory. Consequently we tried to prepare polylanthionine from *meso*-lanthionine itself. Unlike cystine, *meso*-lanthionine did not give the mono-, but exclusively, the *NN'*-di-(benzyloxycarbonyl) derivative. As lanthionine did not yield the dicarboxyanhydride in dioxan this compound was synthesised from the *NN'*-di(benzyloxycarbonyl)-*meso*-lanthionine by reaction with phosphorus pentachloride in ether; it was polymerised in bulk by heating it *in vacuo*, and on its hydrolysis lanthionine was recovered. This polymer too is not satisfactorily defined in structure.

A structurally defined polylanthionine was finally prepared by using mono-*N*-benzyloxycarbonyl-lanthionine monobenzyl ester, which was obtained as follows:

Benzyloxycarbonylaminoacrylic acid[6] was esterified with benzyl alcohol, and L-cysteine was added to the double bond in aqueous alcohol at pH 7—8. One carboxyl and one adjacent amino-group of the lanthionine molecule thus formed were protected, so that only two functional groups remained free. Passing carbonyl chloride into a suspension of this product (I) in dioxan gave its *N*-carboxyanhydride which was polymerised in pyridine solution to a product (II) with a chain length of 19 units.

Similarly, the " adjacent " monomethyl ester of *N*-acetyl-lanthionine was synthesised from methyl acetamidoacrylate and L-cysteine and converted into the *N*-carboxy-anhydride and thence into a polymer (III).

In the present work we also synthesised and polymerised *S*-2-methoxycarbonyl-ethyl-L-cysteine, from methyl acrylate and L-cysteine. The product has structure (III) with the acetamido-group replaced by hydrogen; it has a high decomposition temperature and is insoluble in the ordinary organic solvents.



Experimental

M. p.s were determined in a Fisher–Johns apparatus.

Polymerisation of Mono-N-benzyloxycarbonyl-L-cystine.—Dry carbonyl chloride was passed with stirring for 1 hr. through a suspension of dried mono-*N*-benzyloxycarbonyl-L-cystine[5] (0·75 g.; recrystallised from 25% aqueous acetic acid) in dry dioxan (100 ml.) at 50°. The solution was filtered, then evaporated *in vacuo* at 30°, and the residue was washed with light petroleum several times. It crystallised during several hours at 0° under light petroleum.

[6] Kildisheva, Rasteikene, and Knunyants, *Bull. Acad. Sci. U.S.S.R.*, 1955, 231.

Recrystallisation from ether–light petroleum yielded the N-*carboxyanhydride*, m. p. 30—32° (Found: N, 6·8. $C_{15}H_{16}N_2O_7S_2$ requires N, 7·0%).

Polymerisation was carried out in bulk at 110°/10^{-3} mm. for 30 min., then at 130°/10^{-3} mm. for 2 hr. The *polymer* obtained was purified from acetic acid–water [Found: C, 46·9; H, 4·6; N, 7·4; amino-N (Van Slyke), 0·3. $(C_{14}H_{16}N_2O_5S_2)_{12},H_2O$ requires C, 47·0; H, 4·5; N, 7·8; amino-N, 0·3%].

*Poly-*L*-cystine.*—Poly-(*N*-benzyloxycarbonylcystine) (0·1 g.) was heated in a saturated solution of hydrobromic acid in acetic acid (20 ml.) for 15 min. at 30°, then kept at room temperature for 2 hr. and concentrated in the vacuum first of a water-pump, then of an oil-pump. The residue was extracted with ether, dissolved in a few ml. of water, neutralised with dilute aqueous ammonia, and immediately acidified with glacial acetic acid. The *polycystine* was filtered off and washed with water [Found: C, 31·9; H, 4·7; N, 12·3; S, 28·0. $(C_6H_{10}N_2O_3S_2)_{12},H_2O$ requires C, 32·2; H, 4·5; N, 12·5; S, 28·6%].

NN′-*Dibenzyloxycarbonyl-*L*-cystine Dibenzyl Ester.*—*NN′*-Di(benzyloxycarbonyl)-L-cystine [7] (5·1 g.), freshly distilled benzyl alcohol (4 ml.), and toluene-*p*-sulphonic acid (0·1 g.) in dry benzene (200 ml.) were refluxed for 8 hr. in an azeotropic-distillation apparatus. After extraction with 2% aqueous sodium hydrogen carbonate the solution was washed with water, dried and evaporated *in vacuo*. The NN′-*dibenzyloxycarbonyl-*L*-cystine dibenzyl ester* crystallised slowly (4·2 g.) and had m. p. 79° (from ethyl acetate–light petroleum) (Found: C, 63·0; H, 5·2; N, 3·9; S, 9·3. $C_{36}H_{36}N_2O_8S_2$ requires C, 62·8; H, 5·3; N, 4·1; S, 9·3%).

NN′-*Dibenzyloxycarbonyl-*meso*-lanthionine Dibenzyl Ester.*—*NN′*-Dibenzyloxycarbonyl-*meso*-lanthionine (2·4 g.), freshly distilled benzyl alcohol (2 ml.), and toluene-*p*-sulphonic acid (0·1 g.) in toluene (150 ml.) were refluxed for 8 hr. in an azeotropic distillation apparatus. Magnesium oxide was added (0·5 g.) and the whole shaken and filtered. The toluene was removed at the water-pump, then at the oil-pump. The *dibenzyl ester*, dissolved in acetone and precipitated with water, crystallised gradually (1·4 g., 40%); recrystallised from aqueous ethanol, it had m. p. 90° (Found: C, 65·5; H, 5·7; N, 4·3; S, 5·2. $C_{36}H_{36}O_6N_2S$ requires C, 65·8; H, 5·5; N, 4·3; S, 4·9%).

NN′-*Dibenzyloxycarbonyl-*meso*-lanthionine Diethyl Ester.*—A solution of *meso*-lanthionine (10 g.) in absolute ethanol (200 ml.) was saturated with hydrogen chloride and refluxed (10 hr.). Chromatography in aqueous phenol (80%) showed the presence of only one compound (R_F 0·95), and the absence of free lanthionine. The solution was evaporated at the water-pump, ethanol (50 ml.) added and removed again, and the residue was taken up in water (125 ml.), and treated with, first, magnesium oxide (5 g.) and then an 80% solution of benzyl chloroformate (25 g.) in toluene during 1 hr. with stirring and cooling (ice-bath). Stirring was continued for 2 hr., ether (2 × 50 ml.) being added. The solution was filtered, more ether (50 ml.) added, and the ether layer washed with water, dried, and evaporated. Trituration of the residue with light petroleum gave the *diethyl ester* (19 g., 70%), m. p. 72° (from ether–light petroleum) (Found: N, 5·2; EtO, 16·6. $C_{26}H_{32}N_2O_6S$ requires N, 5·3; EtO, 16·9%).

Di(acid Chloride) of NN′-*Dibenzyloxycarbonyl-*meso*-lanthionine.*—*NN′*-Dibenzyloxycarbonyl-*meso*-lanthionine (2·4 g.) in dry ether (50 ml.) was treated at 0° with phosphorus pentachloride (2 g.) with shaking. The precipitated *dichloride*, when washed with ether and recrystallised from dioxan–ether, had m. p. 75—76° (decomp.), resolidified 90—95° (1·6 g., 60%) (Found: N, 5·4; Cl, 13·4. $C_{22}H_{22}Cl_2O_6N_2S$ requires N, 5·4; Cl, 13·8%).

Polylanthionine.—The preceding dichloride (1 g.) was polymerised by heating in bulk at 10^{-3} mm. for 30 min. at 100° and 1 hr. at 120°. The *polylanthionine* formed a very hard polymer, insoluble in acetic acid, dimethylformamide, and other organic solvents [Found: C, 40·9; H, 5·2; N, 14·5. $(C_6H_8O_2N_2S)_n$ requires C, 41·9; H, 4·7; N, 16·3%].

N-*Benzyloxycarbonyl-lanthionine Monobenzyl Ester.*—Benzyloxycarbonylaminoacrylic acid [8] (12 g.), dry benzene (300 ml.), quinol (0·1 g.), toluene-*p*-sulphonic acid (0·1 g.), and freshly distilled benzyl alcohol (11 g.) were refluxed for 5 hr. in an azeotropic distillation apparatus, then shaken with magnesium oxide, filtered, and evaporated *in vacuo* at room temperature. The residue was taken up in ethanol (50 ml.), added to a solution of cysteine hydrochloride (8 g.) in water (40 ml.) that had been neutralised with N-sodium hydroxide, and stirred for 3 hr. at room temperature under hydrogen, then on a water-bath until it gave a negative reaction with sodium nitroprusside, while the pH was kept at 7—8 by addition of sodium hydroxide solution.

[7] " Biochemical Preparations," Vol. II, p. 75, John Wiley, N.Y., 1952.

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Chromatography showed a compound of R_F 0·9 besides little cystine. The solution was filtered, concentrated *in vacuo* to half its volume, and extracted with ether. On further concentration, an oil separated which solidified to a gelatinous precipitate of N-*benzyloxycarbonyl-lanthionine monobenzyl ester*; this was filtered off and washed with water. It had m. p. 175° after precipitation from pyridine by ether (14 g.) and was soluble in acetic acid, dioxan, and ethanol [Found: C, 58·5; H, 5·6; N, 6·6; amino-N (Van Slyke), 3·2; S, 7·5. $C_{21}H_{24}N_2O_6S$ requires C, 58·3; H, 5·5; N, 6·5; amino-N, 3·2; S, 7·4%].

Poly-(N-*benzyloxycarbonyl-lanthionine Monobenzyl Ester*).—The preceding monobenzyl ester (1·5 g.) in dioxan (50 ml.) was stirred while carbonyl chloride was passed through it for 30 min. at room temperature, then at 50° for 30 min.; after filtration and evaporation *in vacuo*, dioxan was added (25 ml.) and the whole was evaporated again. The residue was washed several times with light petroleum. The *N*-carboxyanhydride obtained was polymerised in dry pyridine (25 ml.) for 24 hr. at room temperature and 8 hr. on the water-bath. The pyridine was driven off *in vacuo* and the *polymer* washed with boiling water and dried. It was soluble in organic solvents and was purified from aqueous ethanol [Found: C, 60·6; H, 5·2; N, 6·5; amino-N (Van Slyke), 0·18; S, 7·4. $(C_{21}H_{22}N_2O_5S)_{19},H_2O$ requires C, 60·7; H, 5·3; N, 6·7; amino-N, 0·18; S, 7·7%].

N-*Acetyl-lanthionine Monomethyl Ester*.—Methyl acetamidoacrylate [8] (5 g.) was added to a solution of L-cysteine (3·2 g.) in water (25 ml.). Carbon dioxide was passed with stirring and N-sodium hydroxide added to give pH 7. After 30 minutes' stirring the temperature was raised to 60° and stirring continued for 2 hr. After extraction with ether the solution was evaporated *in vacuo*, and the residue dissolved in water, filtered, and precipitated with acetone. The precipitate was extracted with ethyl alcohol which on evaporation gave N-*acetyl-lanthionine monomethyl ester* (3 g.), m. p. 80—85°, R_F 0·84—0·86 [Found: C, 41·2; H, 6·4; N, 10·4; amino-N (Van Slyke), 5·2. $C_9H_{16}N_2O_5S$ requires C, 40·9; H, 6·1; N, 10·6; amino-N, 5·3%].

Poly-(N-*acetyl-lanthionine Monomethyl Ester*).—*N*-Acetyl-lanthionine monomethyl ester (0·5 g.) in dioxan (50 ml.) was stirred while carbonyl chloride was passed through it for 90 min. at 50°. The solution was filtered and evaporated *in vacuo*, dioxan (25 ml.) added, and the whole evaporated again. The *N*-carboxyanhydride was washed several times with light petroleum. It was polymerised in bulk at 10^{-3} mm. at 90° for 1 hr. and at 120° for 2 hr. The polymer gave a positive biuret reaction [Found: N, 11·1; amino-N (Van Slyke), 0·4. $(C_9H_{14}N_2O_4S)_{15},H_2O$ requires N, 11·3; amino-N, 0·4%].

S-2-*Methoxycarbonylethyl*-L-*cysteine*.—Methyl acrylate (5·7 g.) was added to a solution of L-cysteine hydrochloride (4·7 g.) in water (10 ml.), hydrogen was passed through it, and N-sodium hydroxide was dropped in with stirring to give pH 7. The solution became hot and crystals separated. Stirring was continued for another hour (to absence of SH). Recrystallisation from 70% ethanol gave S-2-*methoxycarbonylethyl*-L-*cysteine*, m. p. 217° (60%), R_F (80% phenol) 0·82—0·84 (Found: C, 40·8; H, 6·4; N, 6·7; S, 15·2. $C_7H_{13}NO_4S$ requires C, 40·6; H, 6·3; N, 6·8; S, 15·4%).

N-*Benzyloxycarbonyl*-S-2-*methoxycarbonylethyl*-L-*cysteine*.—The preceding acid (1 g.) in water (50 ml.) and ether (25 ml.) was stirred with magnesium oxide (0·5 g.) at 0° and benzyl chloroformate (1 g.) was dropped in. After 30 min. the solution was left at room temperature for 1 hr., then filtered, extracted with ether, and acidified. The oil was removed in ethyl acetate, dried, and recovered *in vacuo*. Triturated with light petroleum it gave N-*benzyloxycarbonyl*-S-2-*methoxycarbonylethyl*-L-*cysteine*, m. p. 63—64° (from ethyl acetate–light petroleum) (1·5 g.) (Found: N, 3·9. $C_{15}H_{19}NO_6S$ requires N, 4·1%).

Poly-(S-2-*methoxycarbonylethyl*-L-*cysteine*).—*S*-2-Methoxycarbonylethyl-L-cysteine (1 g.) in dioxan (50 ml.) was heated at 50° and carbonyl chloride passed in for 1 hr. The solution was filtered and evaporated *in vacuo*. The residue was taken up in dioxan (25 ml.), which was removed again. The *N*-carboxyanhydride was washed with light petroleum and left in a vacuum-desiccator over phosphorus pentoxide. Polymerisation was carried out in bulk at 10^{-3} mm. at 110° for 1 hr. and at 130° for 2 hr. The hard *polymer* was digested with acetic acid and the residue filtered off and dried [Found: C, 44·0; H, 5·5; N, 7·6; S, 16·3. $(C_7H_{11}NO_3S)_n,H_2O$ requires C, 44·4; H, 5·8; N, 7·4; S, 16·9%].

HEBREW UNIVERSITY, JERUSALEM, ISRAEL. [*Received, June 30th*, 1960.]

[8] Rothstein, *J.*, 1949, 1968.

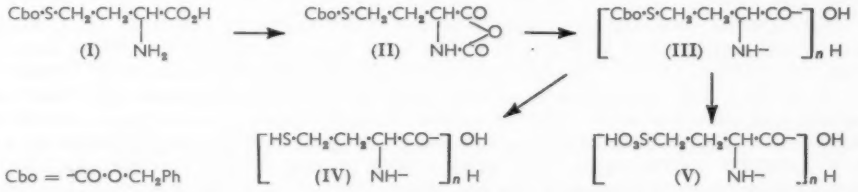
83. *Syntheses of Poly-(S-alkyl-DL-homocysteines), Poly-DL-homocysteine, and Poly-DL-homocysteic Acid.*

By MAX FRANKEL and DAVID GERTNER.

IN continuation of work [1] on the polymerisation of *S*-alkyl-L-cysteines, the polymerisation of *S*-alkyl-DL-homocysteines has been investigated.

The *S*-alkyl-DL-homocysteines were prepared by reducing DL-methionine with sodium in liquid ammonia and treating the homocysteine so prepared with excess of alkyl halides.[2] Passing carbonyl chloride into suspensions of them in dioxan at 50° gave the *N*-carboxyanhydrides which were polymerised in pyridine or dioxan solution or in bulk. Most of these polymers are more soluble in acetic acid, pyridine, and dimethylformamide than their lower homologues, the poly-(*S*-alkyl-L-cysteines).

Attempts to prepare poly-DL-homocysteine by reduction of poly-(*S*-benzyl-DL-homocysteine) with sodium in liquid ammonia gave impure products, so poly-DL-homocysteine was synthesised from poly-(*S*-benzyloxycarbonyl-DL-homocysteine) which was reduced more satisfactorily.[3] *S*-Benzyloxycarbonyl-DL-homocysteine (I) was prepared by the action of 1 mol. of benzyl chloroformate on DL-homocysteine in sodium hydrogen carbonate solution and was polymerised *via* its *N*-carboxyanhydride (II). Reduction of the resulting



polymer (III) yielded poly-DL-homocysteine (IV); this gave a positive nitroprusside reaction, and iodometric titration of the thiol groups showed the presence of 95% of the calculated amount. Oxidation of the polymer (III) in formic acid solution by excess of hydrogen peroxide gave poly-DL-homocysteic acid (V), hydrolysis of which by 20% hydrochloric acid gave only homocysteic acid.

Experimental. M. p.s were determined in a Fisher–Johns apparatus. The ascending method of paper chromatography in 80% phenol was used.

S-*Benzyloxycarbonyl*-DL-*homocysteine* (I). To DL-homocysteine (6·7 g.) dissolved in N-sodium hydrogen carbonate (75 ml.) at 0° benzyl chloroformate (8 g.) in ether (25 ml.) was added during 30 min. with stirring, which was continued for 1 hr.; then more ether (25 ml.) added and the whole stirred for a further 3 hr. The precipitate was filtered off and washed with ether, followed by water (yield, 2·9 g., 20%; R_F 0·92; m. p. 230° on recrystallisation from water). If the filtrate was stirred for a further 3 hr. the total yield of S-*benzyloxycarbonyl*-DL-*homocysteine* was 35% [Found: C, 53·6; H, 5·8; N, 5·2; amino-N (Van Slyke), 5·2; S, 11·2. $C_{12}H_{15}NO_4S$ requires C, 53·5; H, 5·6; N, 5·2; amino-N, 5·2; S, 11·9%].

NS-*Dibenzyloxycarbonyl*-DL-*homocysteine*. To a solution of DL-homocysteine (6·8 g.) in 2N-sodium hydroxide (25 ml.) at 0° benzyl chloroformate (18 g.) and 2N-sodium hydroxide (50 ml.) were simultaneously added with stirring which was then continued for 2 hr. The solution was extracted with ether and acidified with hydrochloric acid. The NS-*dibenzyloxycarbonyl*-DL-*homocysteine* which separated as an oil crystallised at 0° and was filtered off and washed with water; it (15 g., 75%) had m. p. 72—74° on recrystallisation from carbon tetrachloride (Found: N, 3·7. $C_{20}H_{21}NO_6S$ requires N, 3·5%).

N-*Carboxyanhydride of* S-*benzyloxycarbonyl*-DL-*homocysteine* (II). Dry carbonyl chloride

[1] Frankel, Gertner, Jacobson, and Zilkha, *J.*, 1960, 1390.
[2] Armstrong and Lewis, *J. Org. Chem.*, 1951, **16**, 749.
[3] Berger, Noguchi, and Katchalski, *J. Amer. Chem. Soc.*, 1956, **78**, 4483.

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was passed with stirring into a suspension of the acid (I) (1·2 g.) in dry dioxan (50 ml.) at room temperature for 90 min. The filtered solution was evaporated *in vacuo* at 30—40°, and the residue dissolved in dioxan (25 ml.) and evaporated once more. The N-*carboxyanhydride*, recrystallised from ether–light petroleum, had m. p. 75—76° (Found: N, 4·7. $C_{13}H_{13}NO_5S$ requires N, 4·7%).

Poly-(S-*benzyloxycarbonyl*-DL-*homocysteine*) (III). Dry, freshly recrystallised *N*-carboxyanhydride (II) (0·5 g.) was dissolved in pyridine (10 ml.) and left for 2 days at room temperature, then heated on a water-bath for a few hr. The pyridine was evaporated *in vacuo*, and the residue washed with water and dried. The *polymer* was purified by dissolving it in a small volume of pyridine and reprecipitating it with ether. It is soluble in acetic acid, gives a positive biuret reaction, and softens around 160° [Found: C, 57·2; H, 5·3; N, 5·7; S, 12·1; amino-N (Van Slyke), 0·1. $(C_{13}H_{13}NO_3S)_{50},H_2O$ requires C, 57·3; H, 5·2; N, 5·6; amino-N, 0·1; S, 12·7%].

Poly-DL-*homocysteine* (IV). Poly-(*S*-benzyloxycarbonyl-DL-homocysteine) (III) (0·5 g.) was suspended in liquid ammonia and sodium metal in small pieces added slowly with stirring until the blue colour persisted. A little ammonium chloride was added (to disappearance of the colour). The ammonia was evaporated at room temperature and then *in vacuo*. Boiled water (10 ml.) was added to the residue and the solution twice centrifuged. The aqueous solution was extracted with ether and acidified with hydrochloric acid. The *polymer* was collected, washed with water, and dried (yield 0·15 g.) (care has to be taken to prevent exposure to air to avoid oxidation) [Found: C, 41·2; H, 6·1; N, 11·8. $(C_4H_7NOS)_n,H_2O$ requires C, 41·0; H, 6·0; N, 12·0%].

Poly-DL-*homocysteic acid* (V). Poly-(*S*-benzyloxycarbonyl-DL-homocysteine) (III) (0·5 g.) was treated in 90% formic acid (25 ml.) with 30% hydrogen peroxide (2 ml.), with stirring for 2 hr. at room temperature. Evaporation to dryness *in vacuo*, dissolution of the residue in water (25 ml.), and evaporation to dryness again gave *poly*-DL-*homocysteic acid* which was washed with ether and dried. It gives a positive biuret reaction, is hygroscopic, soluble in water, acetic acid, and insoluble in acetone, and softens at 110° [Found: C, 29·8; H, 4·7; N, 8·5; S, 19·0. $(C_4H_7NO_4S)_{50},H_2O$ requires C, 29·1; H, 4·3; N, 8·5; S, 19·4%]. Titration of the polymer with 0·1N-sodium hydroxide (Bromophenol Blue) showed 92% of the calculated sulphonic groups.

S-*Benzoyl*-DL-*homocysteine*. To DL-homocysteine (6·7 g.) in N-sodium hydrogen carbonate (50 ml.) at 0° benzoyl chloride (7 g.) in ether (25 ml.) was added with stirring simultaneously with further N-sodium hydrogen carbonate solution (50 ml.). After 2 hr. the precipitate of S-*benzoyl*-DL-*homocysteine* was filtered off and washed with cold water, ethanol, and ether (yield 3·5 g., 30%). It had m. p. 210° (recrystallised from water) and gave a negative nitroprusside reaction (on storage, a weak colour developed) (Found: C, 55·3; H, 5·4; N, 5·8; S, 13·2. $C_{11}H_{13}NO_3S$ requires C, 55·3; H, 5·5; N, 5·9; S, 13·4%).

N-*Carboxyanhydride of* S-*benzoyl*-DL-*homocysteine*. The *N*-carboxyanhydride, prepared as above in 80% yield and recrystallised from ether–light petroleum, had m. p. 95—96° (Found: N, 5·1. $C_{12}H_{11}NO_4S$ requires N, 5·3%).

Poly-(S-*benzoyl*-DL-*homocysteine*). The preceding *N*-carboxyanhydride (0·2 g.) was left in dry dioxan (15 ml.) with triethylamine (0·05 ml.) for 18 hr. at room temperature and then for 6 hr. on a boiling-water bath. The dioxan was removed *in vacuo*. The residual *poly*-(S-*benzoyl*-DL-*homocysteine*) gave a positive biuret reaction and was soluble in hot glacial acetic acid and dimethylformamide [Found: C, 59·8; H, 5·2; N, 6·3; amino-N (Van Slyke), 0·1. $(C_{11}H_{11}NO_3S)_{60},H_2O$ requires C, 59·6; H, 5·0; N, 6·3; amino-N, 0·1%].

Poly-(S-*benzyl*-DL-*homocysteine*). *S*-Benzyl-DL-homocysteine was prepared by an exchange reaction of benzyl chloride with DL-methionine.[4] The *N*-carboxyanhydride was prepared as usual but in dry tetrahydrofuran (50 ml. per g.) for 1 hr. The solution was evaporated *in vacuo*, and the residue dissolved in tetrahydrofuran (25 ml.) and evaporated again. The N-*carboxyanhydride*, recrystallised from ether–light petroleum, had m. p. 57° (Found: N, 5·6. $C_{12}H_{13}NO_3S$ requires N, 5·6%).

Polymers were obtained from the *N*-carboxyanhydride in a high vacuum and in pyridine [Found, for polymer prepared *in vacuo*: C, 63·5; H, 6·3; N, 6·8; S, 15·2. $(C_{11}H_{13}NOS)_n,H_2O$ requires C, 63·8; H, 6·3; N, 6·8; S, 15·5. Found, for polymer prepared in pyridine: N, 6·6%].

[4] Dekker and Fruton, *J. Biol. Chem.*, 1948, **173**, 471.

Poly-(S-*allyl*-DL-*homocysteine*). The *N*-carboxyanhydride was prepared from *S*-allyl-DL-homocysteine as above and polymerised in pyridine. The *polymer* is soluble in acetic acid and gave a positive biuret reaction [Found: C, 53·4; H, 7·1; N, 8·7; amino-N (Van Slyke), 0·1. $(C_7H_{11}ONS)_{90},H_2O$ requires C, 53·4; H, 7·0; N, 8·9; amino-N, 0·1%].

Poly-(S-*ethyl*-DL-*homocysteine*) (*poly*-DL-*ethionine*). The *N*-carboxyanhydride was prepared from DL-ethionine and polymerised in pyridine and in dioxan. The *polymer* from pyridine was recovered on evaporation *in vacuo* and trituration of the residue with ethanol [Found, for the pyridine polymer: C, 49·4; H, 7·4; N, 9·4; S, 21·6. $(C_6H_{11}ONS)_n,H_2O$ requires C, 49·7; H, 7·6; N, 9·7; S, 22·1%. Found, for the dioxan polymer: N, 9·5%].

Poly-(S-*propyl*-DL-*homocysteine*). The *polymer* was prepared from the *N*-carboxyanhydride of *S*-propyl-DL-homocysteine obtained as above, which was polymerised in pyridine [Found: N, 8·6; amino-N (Van Slyke), 0·2. $(C_7H_{13}ONS)_{45},H_2O$ requires N, 8·8; amino-N, 0·2%].

Poly-(S-*butyl*-DL-*homocysteine*) (*poly*-DL-*butionine*). *Poly*-(S-*butyl*-DL-*homocysteine*) was prepared *via* the *N*-carboxyanhydride by polymerisation in pyridine [Found: C, 55·7; H, 8·8; N, 7·9. $(C_8H_{15}ONS)_n,H_2O$ requires C, 55·5; H, 8·7; N, 8·1%].

Note. In calculating analytical detail for the indefinite polymers, n was taken as ∞ and the end-group (H_2O), being insignificant, was neglected.

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84. *A Grignard Reagent from* p-*Bromodimethylaniline.*

By T. C. OWEN.

THE preparation of an ethereal Grignard reagent from *p*-bromodimethylaniline is difficult [1] but a moderately successful preparation has been described by Davies and Mann.[2] In tetrahydrofuran [3] reaction proceeds smoothly and the reagent so obtained may be used to prepare *p*-dimethylaminobenzoic acid in excellent yield.

Experimental.—*p*-Bromodimethylaniline (15 g.) reacted exothermally with magnesium (excess) in tetrahydrofuran (100 ml.) after initiation by a little ethyl iodide or iodine. Reaction was completed by 30 minutes' refluxing. Part (5 ml.) of the solution was added, after cooling, to solid carbon dioxide. More tetrahydrofuran (5 ml.) was added, followed by 2% acetic acid (55 ml.). The precipitate was recrystallised from etnanol, affording *p*-dimethylaminobenzoic acid (88%), m. p. and mixed m. p. 243° (Found: equiv., 165. Calc. for $C_8H_{10}N{\cdot}CO_2H$: equiv., 165) (Me ester, m. p. 102°).

Commercial (British Drug Houses Ltd.) tetrahydrofuran was freed from peroxides by refluxing it over aqueous ferrous sulphate acidified with sulphuric acid, then distilled through a short column of glass beads, dried (2 portions of $CaCl_2$), refluxed over and distilled from sodium wire, and stored over fresh sodium wire in a dark bottle.

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[1] See, *e.g.*, Kharasch and Reinmuth, "Grignard Reactions of Non-metallic Substances," Prentice-Hall, Constable, London, 1954, pp. 10—11, 41, 404, 896; Baeyer and Villiger, *Ber.*, 1903, **36**, 2794; Chamberlain and Dull, *J. Amer. Chem. Soc.*, 1928, **50**, 3088.

[2] Davies and Mann, *J.*, 1944, 276.

[3] Cf., *e.g.*, Normant, *Compt. rend.*, 1954, **239**, 1510; Rosenberg, Gibbons, and Ramsden, *J. Amer. Chem. Soc.*, 1957, **79**, 2137; Metal and Thermit Corp., B.P. 776,933.

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85. *The Conductance of Ferric and Cupric Stearates in Aliphatic Hydrocarbons.*

By C. M. French and E. R. Monks.

An attempt was recently made, using a Schering a.c. bridge, to investigate the conductometric behaviour of 10^{-3}—10^{-5}M-solutions in repeatedly fractionated n-heptane, n-decane, and n-dodecane of anhydrous and moist (2 molecules of water per metal atom) cupric and ferric stearate purified by recrystallisation. The specific conductances of the solvents were less than 4×10^{-14} ohm^{-1} cm.$^{-1}$, their dielectric constants between 1·93 and 2·14, and their viscosities between 0·24 and 1·14 centipoise. Conductances were not reproducible to a high degree of accuracy and, in the case of measurements at more than one temperature, depended on the rate of cooling. Equilibrium was attained very slowly, in some cases only after several hours. Similar observations have been recorded earlier [1,2] for analogous measurements on systems of this type, and are probably associated with a slow ionisation of the solute molecules, a slow exchange of ions and molecules between micelles formed by the solute, and variations in micelle structure. In each case in the present work, conductances were measured first at 65° and then at progressively lower temperatures, measurements being started 20 min. after the sample had been placed in the thermostat-bath at each selected temperature. In spite of very extensive precautions there was a considerable scatter of results and lack of reproducibility with some systems, and only the more distinct features, as summarised below, will therefore be reported.

(1) Conductances of all solutions were very much greater than those of the pure solvents (molar conductances of solutions were between 10^{-4} and 10^{-6} ohm^{-1} cm.^{2}), indicating that ionisation, though not extensive, does occur in these solutions.

(2) The molar conductances of all solutions of ferric stearate were greater (up to 10-fold for anhydrous, and up to 100-fold for moist, solutions) than those of the same concentration of cupric stearate.

(3) Addition of 2 moles of water per mole of solute had little effect on the conductance of cupric stearate, but caused a significant (up to 10-fold) increase in that of ferric stearate solutions.

(4) Change of solvent had only a small effect on the conductance of either salt, heptane solutions being somewhat more conducting than those in the other two, more viscous solvents.

(5) Increase in temperature generally resulted in the usual increase in conductance, although some anhydrous solutions at concentrations greater than 10^{-3}M had lower conductances at 65° than at 45°.

(6) Plots of the molar conductance Λ_m of the cupric stearate solutions against $c^{\frac{1}{2}}$ gave curves with either clear minima or indications that one would occur at a concentration slightly greater than that measured here, and a typical example is shown in Fig. 1. In anhydrous solutions, increasing the dielectric constant of the solvent results in the expected shift of the minimum to higher concentrations, but little change occurs in the moist solutions. At concentrations below the conductance minimum, log Λ_m–log c plots were in many cases linear, with slope $-\frac{1}{2}$. There are thus indications of the formation of both ion-pairs and triple ions in these systems. Measurements in ferric stearate solutions were the least reproducible, but one clear feature was the presence of a maximum as well as a minimum, or a tendency towards one, in the conductance–concentration curves for the moist solutions (Fig. 2), although it is possible that this was due to some of the solute passing into colloidal rather than true solution at higher concentrations.

The lack of uniformity in conductometric behaviour from system to system is undoubtedly associated with the formation of micelles by the solute molecules in the

[1] Nelson and Pink, *J.*, 1954, 4412.
[2] Nesbitt and Pink, 2nd Internat. Congress Surface Activity, 1957, Vol. III, p. 13.

hydrocarbons, and the adsorption of ions on them. A complex pattern of behaviour may be expected, especially as concentration and temperature are varied. Among the factors to be noted which may influence the number and nature of conducting particles present are the series of equilibria of the type suggested by Burkin,[3] which, for the salt of an " *n* "-valent metal M, may be represented as:

$$MR_n \rightleftharpoons (MR_{n-1})^+ + R^-$$
$$xMR_n \rightleftharpoons (MR_n)_x \rightleftharpoons [(MR_n)_xMR_{n-1}]^+ + [(MR_n)_xR]^-$$

The degree of aggregation x will depend on solute and solvent, and will increase with increase in concentration and decrease in temperature. However, the close proximity of

FIG. 1. Λ_m–$c^{\frac{1}{2}}$ *plot for cupric stearate " dihydrate " in n-decane at* (A) 25°, (B) 45°, *and* (C) 65°.

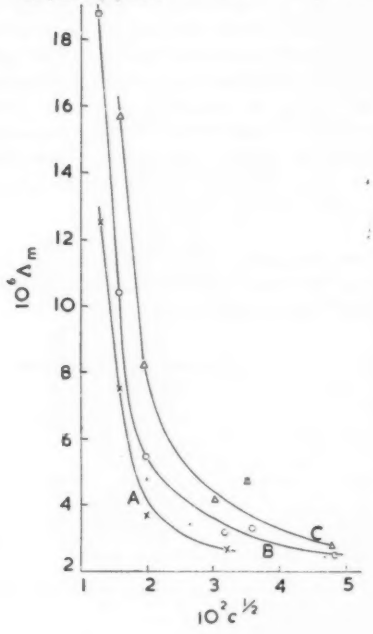
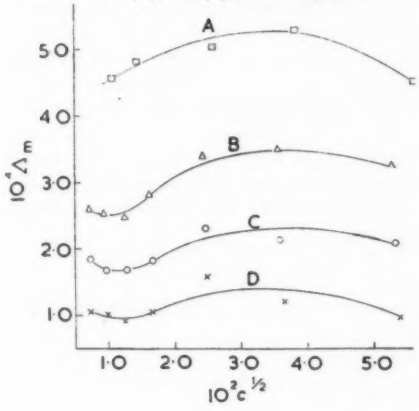


FIG. 2. Λ_m–$c^{\frac{1}{2}}$ *plot for ferric stearate " dihydrate ": (A) in n-heptane at* 45°; *and in n-decane at* (B) 65°, (C) 45°, *and* (D) 25°.



metal–carboxyl groups in the micelles would tend to increase ionisation in the micelles as compared with single molecules, and hence lead to an increase in conductance with increase in micellar complexity. This effect is opposite in direction to, and would be superimposed on, the normal ones resulting from temperature and concentration changes.

Such changes as the addition of small traces of water may bring about in the conductance of the present systems are probably to be ascribed to hydration of the solute molecules and their subsequent hydrolysis rather than to any changes in the dielectric constant of the medium. Again, however, a series of complex equilibria is possible, and until more precise data can be obtained with these systems attempts at detailed analysis of the results would be unprofitable.

The same factors would be expected to operate in solutions of these solutes in mixtures

[3] Burkin, *J.*, 1954, 71.

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of hydrocarbons, and as expected, the conductometric behaviour of solutions of cupric and ferric stearates in three mixtures of heptane and dodecane follow the same general pattern as in single pure hydrocarbons. Such additional features as the commonly somewhat lower conductance in the mixed solvent than in the single constituent hydrocarbons, and the slightly greater variation in conductance on change of solvent, which was not always in the direction expected from the viscosity change, were not sufficiently well defined to be capable of analysis in these complex systems.

Finally, as might be expected, the conductometric behaviour of solutions, in n-heptane, of mixtures of cupric and ferric stearate did not differ markedly from that of the other systems, although the Λ_m–$c^{\frac{1}{2}}$ curves were as a rule shallower and with less pronounced minima, and the conductances of all the anhydrous mixtures were less than those of the same concentration of ferric or of cupric salt alone. Conductances of moist mixtures were less than those of moist ferric stearate solutions in heptane. The conductance of anhydrous solute mixtures also decreased to a minimum as the composition of the solute reached equimolecular proportions, although an increase in conductance with change in solute composition was only observed in the moist solutions when the proportion of ferric stearate was more than 50% molar. The last phenomenon may also be associated with the nature of the solutes, Lawrence [4] having reported the occurrence of mutual peptisation of soaps in solutions containing mixtures of these solutes in non-polar solvents. This effect, with the consequent decrease in aggregation of solute molecules, would be expected to be a maximum for equimolecular mixtures, and also to reduce aggregation below that for a single pure solute of the same concentration. The observed conductance changes are thus not incompatible with these views on the nature of the solutions.

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[*Received, April 11th,* 1960.]

[4] Lawrence, *J. Phys. Colloid Chem.*, 1948, **52**, 1510.

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86. *Surface Tensions of Some Molten Metal Nitrates and Nitrites.*

By C. C. ADDISON and J. M. COLDREY.

BECAUSE of their advantages as high-temperature solvents and reaction media, molten salts (particularly nitrates and chlorides) are being studied extensively, and their electrical properties, density, viscosity, vapour pressure, etc., interpreted in terms of ion association in the melt. Surface tension is also a sensitive measure of ion association, but has been less fully studied. This Note records the first measurements of the surface tensions of calcium, strontium, and barium nitrates; values for certain alkali-metal nitrates [and for silver, thallium(I), and ammonium nitrates], for which published data are scanty, have been redetermined. The surface tensions of sodium and potassium nitrites have been determined over a temperature range for comparison with the nitrates, since decomposition of molten nitrates usually produces nitrite in solution.

Experimental.—Surface tensions were measured by the maximum bubble pressure method by use of the apparatus shown in Fig. 1, and argon (British Oxygen Co. 99·98%) purified by

passage through Linde molecular sieve, grade 4A. The containing vessel and orifice tube were of Supremax glass, which showed no deformation below 750°. The orifice tube passed down the centre of the delivery tube (A) through which argon also passed continuously to provide a blanket of inert gas. Vertical movement of A and the orifice tube was controlled by a fine screw thread and vernier. Orifices of approx. 0·08 cm. internal diameter were used, and results calculated by using Sugden's correction factors.[1] The lagged steel furnace B (controlled by thermocouple T to $\pm 1°$) carried observation holes protected by mica windows through which bubble formation was observed; bubbles formed cleanly on the inside edge of the orifice. In most cases, tension values were determined at zero and at finite depths of immersion, and during both heating and

FIG. 1. *Apparatus for determination of surface tension.*

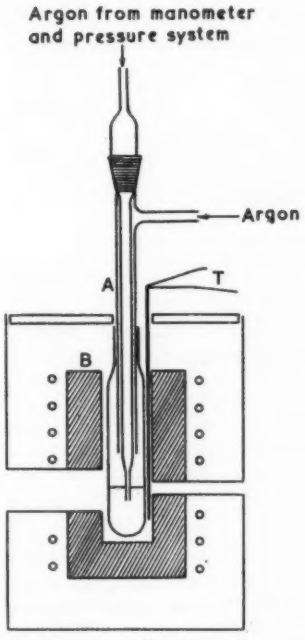
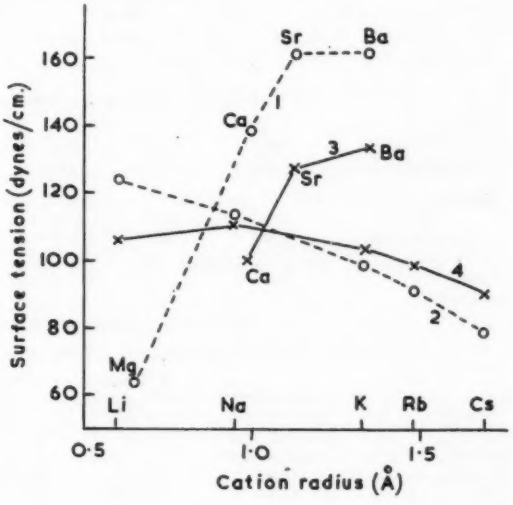


FIG. 2. *Surface tensions of molten Group I and Group II chlorides and metal nitrates.* (1) *Group II chlorides at* 1000°. (2) *Group I chlorides at* 800°. (3) *Group II nitrates at* 595° (Ba), 615° (Sr), *or* 560° (Ca). (4) *Group I nitrates at* 425°.



cooling of the melt. Results were reproducible within $\pm 0·5$ dyne/cm. The apparatus was calibrated by using molten " AnalaR " sodium and potassium nitrates. The values given in Table 3, for comparison with the nitrites, are in good agreement with accepted values.[2-6]

Barium, silver, and ammonium nitrates, and sodium nitrite, were of " AnalaR " grade. The remainder were of reagent grade. The only salt containing appreciable impurity was potassium nitrite. Analysis for NO_2^- gave 95·3% purity; the remainder was nitrate and had a negligible effect on the surface tension of the nitrite (Table 3). The anhydrous salts were dried at 110° for several hours before use.

[1] Sugden, *J.*, 1922, **121**, 858.
[2] Jaeger, *Z. anorg. Chem.*, 1917, **101**, 1.
[3] Semenchenko and Shikhobalova, *Mineral Suir'e*, 1936, **11**, 27.
[4] Boardman, Palmer, and Heymann, *Trans. Faraday Soc.*, 1955, **51**, 277.
[5] Gromakev and Kostromin, *Uchenye Zapiski Kazan, Gosudarst. Univ. im. V.I. Ul'yanova-Lenina, Khim*, 1955, **115**, 93.
[6] Dahl and Duke, U.S.A.E.C., Publ. No. ISC–923, 1958.

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Results. The liquid temperature range available with the alkaline-earth nitrates increases with atomic weight of the metal. The behaviour of the melts may be summarised as follows:

	$Ca(NO_3)_2$	$Sr(NO_3)_2$	$Ba(NO_3)_2$
Clear, pale amber liquid, gas evolution negligible	555°	605°	595°
Small gas bubbles perceptible in melt	560	615	630
Gas evolution sufficient to interfere with tension measurement ...	575	635	675

Anhydrous magnesium nitrate decomposes almost immediately on melting. Only with barium nitrate was a determination of temperature coefficient feasible; results are given in Table 1. These values were unchanged when the melt was kept for some hours, even at 660°, so that the surface tension of molten barium nitrite must be very near to that of the nitrate. This is certainly the case for sodium and potassium nitrites (Tables 2 and 3).

TABLE 1. *Surface tension of molten barium nitrate.*

	Surface tension (dynes/cm.) *				Surface tension (dynes/cm.) *		
Temp.	(*a*)	(*b*)	(*c*)	Temp.	(*a*)	(*b*)	(*c*)
600°	134·6	134·4	134·8	640°	133·9	134·0	—
620	134·5	134·4	134·4	660	133·7	133·6	133·8

* Depth of orifice immersion: (*a*) 0·5 cm., (*b*) 1·0 cm., (*c*) 1·5 cm.

TABLE 2. *Surface tensions of molten nitrites.*

$NaNO_2$						
Temp.	291°	308°	334°	355°	367°	384°
γ (dynes/cm.)	120·2 *	120·0	118·9	118·0 *	117·6	116·8 *

KNO_2							
Temp.	445°	460°	470°	474°	480°	487°	501°
γ (dynes/cm.)	106·7 *	106·5	105·5 *	105·1	104·4 *	104·0	103·7 *

* Determined during the heating cycle: other values determined during subsequent cooling of the melt.

TABLE 3. *Surface tension constants.*

[$\gamma = \alpha - \beta(t - t_0)$, where t_0 = m. p. of salt.]

Salt	t_0	α (dynes/cm.) (γ at m. p.)	β (temp. coeff., dynes cm.$^{-1}$ deg.$^{-1}$)	Temp. range used	Lit. values (refs. in parentheses) α	Lit. values (refs. in parentheses) β
$Ca(NO_3)_2$ ...	551°	101·5 (at 560°)	—	—	—	—
$Sr(NO_3)_2$ ...	605	128·4 (at 615°)	—	—	—	—
$Ba(NO_3)_2$ ...	595	134·8	0·015	600—660°	—	—
$LiNO_3$	255	115·4	0·053	276—425	117·7 [2]	0·061 [2]
$RbNO_3$ ...	306	—	—	—	109·0 [3], 109·1 [5]	0·074 [3], 0·070 [5]
$CsNO_3$	414	92·5	0·069	421—597	92·3 [3]	0·083 [3]
$AgNO_3$	212	152·1	0·082	244—400	149·9 [6], 170·2 [2]	0·069 [6], 0·082 [2]
$TlNO_3$	206	94·8	0·078	226—458	118·3 [3]	0·084 [3]
NH_4NO_3 ...	170	101·9	0·105	170—220	99·5 [7]	0·062 [7]
$NaNO_3$ ...	277	121·2	0·041	291—384	119·6,[9] 124·5,[10] 122·7 [8]	0·07,[10] 0·028 [9]
$NaNO_3$ ...	308	116·6	0·050	320—500	116·9 [4] [9]	0·057 [4] [9]
KNO_3	435	107·6	0·080	445—501	109·3 [8]	—
KNO_3	334	110·8	0·073	350—520	109·9 [4] [9]	0·073 [4] [9]

With all salts studied, surface tension varied linearly with temperature. The results are therefore given in Table 3 in terms of constants for the appropriate equations. The α values for lithium and cæsium nitrates confirm the single published values by Jaeger [2] though β differs somewhat. Jaeger's values [2] for the surface tension of thallous nitrate, however, are much higher than ours.

[7] Rehbinder, *Z. phys. Chem.*, 1926, **121**, 103.
[8] Traube, *Ber.*, 1891, **24**, 3074.
[9] Bloom, Davis, and James, *Trans. Faraday Soc.*, 1960, **56**, 1179.
[10] Frame, Rhodes, and Ubbelohde, *Trans. Faraday Soc.*, 1959, **55**, 2039.

The significance of the surface-tension values for the molten salts of the metals of Groups I and II, in terms of ion-association, is clear from Fig. 2, in which the tensions for molten chlorides and nitrates are plotted against the ionic radius of the cations. The surface tension of the alkali-metal chlorides increases with decreasing ionic radius of the cation, and since covalency in these salts will reduce surface tension, one important factor responsible for the curvature of this graph at low ionic radii may well be the increasing covalency in the liquid state. It is noteworthy that this effect is much more pronounced in the molten nitrates, even when temperature difference is allowed for, and the surface tension of lithium nitrate is less than that for sodium nitrate at all temperatures. With the Group II metal chlorides the influence of cation radius is more than offset by the decrease in tension resulting from covalency, so that surface tensions actually decrease with decreasing cation radius. We now see that the Group II metal nitrates behave similarly, so that covalency is also pronounced in the molten nitrates.

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THE UNIVERSITY, NOTTINGHAM. [*Received, May 9th,* 1960.]

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87. *The Infrared Spectra of Cobalt*(III) *Ethylenediamine Complexes. Part II.*[1] *Compounds containing the Thiocyanate Group.*

By M. E. BALDWIN.

THE infrared spectrum of the thiocyanate ion is characterised by three fundamental modes:[2] the C–N stretching mode ν_1 which occurs near 2050 cm.$^{-1}$, the doubly degenerate bending mode ν_2 near 480 cm.$^{-1}$, and the C–S stretch ν_3 at 750 cm.$^{-1}$.[3]

Cobalt(III)–ethylenediamine complexes containing ionic and co-ordinated thiocyanate have been examined in Nujol mulls in the region 2—20 μ. The absorption bands due to the thiocyanate group have been deduced by comparing the spectra of the complexes containing thiocyanate with those of the *cis*- and *trans*-[Co en_2Cl_2]Cl given in Part I.[1] A number of the compounds were soluble in *NN*-dimethylformamide which was a useful solvent for the study of the C–N stretching region.

The frequencies recorded for the thiocyanate ion in complexes of the type [Co en_2XY]SCN were in good agreement with those found by Jones [3] for potassium thiocyanate and by Chamberlain and Bailar [4] for similar cobalt complexes. The C–S stretching frequency occurs in a region where there are bands due to the rocking of the ethylenediamine-NH_2 groups. On deuteration the NH_2 rocking frequency is shifted while the C–S stretching frequency is unaffected. The assignment of the C–S stretching band was confirmed from the unshifted bands in the spectra of three deuterated complex thiocyanate salts: *trans*-[Co en_2Cl_2]SCN, *trans*-[Co en_2NCS(OH)]SCN, and [Co en_3]$(SCN)_3$ (see Table 1).

The frequencies of absorption bands due to the co-ordinated isothiocyanate group in compounds of the type [Co en_2(NCS)Y]Z are given in Table 2.

Chamberlain and Bailar have assigned a band in the region of 780 cm.$^{-1}$ to the C–S stretch of the isothiocyanato-group in complexes of this type. A comparison of the spectra of compounds containing the isothiocyanato-ligand with those of the *cis*- and *trans*-[Co en_2Cl_2]$^+$ cations indicates that the band in the region of 830 cm.$^{-1}$ is due to the isothiocyanato-group, while that in the 780 cm.$^{-1}$ region is due to a vibration of the NH_2 group. Confirmation of these assignments was obtained by the deuteration of *trans*-[Co en_2(NCS)OH]SCN.

[1] Part I, Baldwin, *J.*, 1960, 4369.
[2] Herzberg, "Infrared and Raman Spectra," Van Nostrand, New York, 1945, p. 174.
[3] Jones, *J. Chem. Phys.*, 1956, **25**, 1069.
[4] Chamberlain and Bailar, *J. Amer. Chem. Soc.*, 1959, **81**, 6412.

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TABLE 1. *Frequencies (cm.$^{-1}$) of absorption bands due to the thiocyanate ion in compounds of the type* [Co en$_2$XY]SCN.

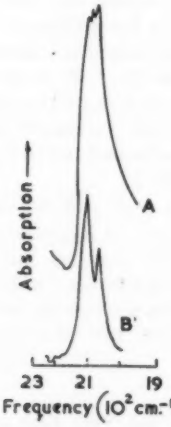
Complex cation	ν_1 (mull)	ν_1 (soln.)	$2\nu_2$	ν_3
trans-[Co en$_2$Cl$_2$]$^+$	2046	—	939, 927	754
trans-[Co en$_2$Cl$_2$]$^+$ (D)	2053			758
trans-[Co en$_2$NCS(Cl)]$^+$	2053	2058	936	730
trans-[Co en$_2$NCS(OH)]$^+$	2041	2058	945	740
trans-[Co en$_2$NCS(OH)]$^+$ (D)	2041			735
trans-[Co en$_2$(NCS)$_2$]$^+$	2070 [a]	2058	943	764
cis-[Co en$_2$Cl$_2$]$^+$	2058		938, 930	746
cis-[Co en$_2$NCS(NO$_2$)]$^+$	2045	2053	963, 935	755
cis-[Co en$_2$Cl(NO$_2$)]$^+$	2070		954, 928	752
[Co en$_3$]$^{3+}$	2066, 2033	2053	945, 926	757, 745
[Co en$_3$]$^{3+}$ (D)	2053, 2008			756, 743

D = deuterated complex. [a] See Fig.

TABLE 2. *Frequencies (cm.$^{-1}$) of absorption bands attributed to the* –NCS *group in compounds of the type* [Co en$_2$(NCS)Y]Z.

Confign.	Y	Z	ν_1 (mull)	ν_1 (soln.)	ν_2
trans	Cl	SCN	2137	2105	833
trans	Cl	S_2O_6	2132, 2088		833
trans	NCS	NO_2	2110		836
trans	NCS	Cl	2119		840
trans	OH	SCN	2128	2105	833
trans	NCS	SCN	2105	2101	835
cis	Cl	Cl	2141		824
cis	Cl	ClO_4	2128		826 [a]
cis	NCS	Cl	2141, 2110		833, 823
cis	NCS	NO_2	2123		835, 824
cis	NO_2	NO_2	2167, 2137	2110	[b]
cis	NO_2	SCN	2128	2114	[b]
cis	OH_2	S_2O_6	2146		833

[a] Reported by Chamberlain and Bailar [4] to be obscured by the broad absorption of the ClO_4^- ion; however, ClO_4^- shows no absorption between 1000 cm.$^{-1}$ and the very strong band at 620 cm.$^{-1}$.[5] [b] Obscured by the strong absorption band of the co-ordinated nitro-group.[6]



trans-[Co en$_2$(NCS)$_2$]SCN: (A) *solid mull*; (B) *solution in* NN-*dimethylformamide*.

[5] Miller and Wilkins, *Analyt. Chem.*, 1952, **24**, 1253.
[6] Chatt, Duncanson, Gatehouse, Nyholm, Tobe, Todd, and Venanzi, *J.*, 1959, 4073.

In trisethylenediaminecobalt(III) thiocyanate, the N–C stretching frequency is split into two sharp bands occurring at 2033 and 2066 cm.$^{-1}$. In solution in *NN*-dimethylformamide only one band at 2053 cm.$^{-1}$ is observed. Similarly, in the solid mull, *trans*-[Co $en_2(NCS)_2$]SCN shows at least three bands close together at 2105, 2092, and 2070 cm.$^{-1}$. In solution the bands due to the N–C stretching in both the ionic and the co-ordinated thiocyanate appear at their characteristic frequencies, *viz.*, 2101 and 2058 cm.$^{-1}$ (see Figure).

BEDFORD COLLEGE, REGENT'S PARK, N.W.1. [*Received, May 31st,* 1960.]

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88. *The Formation of Ferrocenium Thiocyanate in Mixed Aqueous Solvents.*

By T. D. SMITH.

ADDITION of ammonium thiocyanate to a solution of ferrocenium perchlorate in various non-aqueous solvents leads to the formation of a highly coloured, stable complex, though no reaction occurs in water. Adding of water destroys the colour owing to dissociation of the complex.

The ion $Fe(SCN)^{2+}$, though readily formed in water, is also affected by solvent composition, and it has been suggested [1] that the increase in absorption of its aqueous solution with increasing concentration of acetone was due to the lower dielectric constants of the mixed media. Further, in solutions containing a large excess of thiocyanate, complexes of iron(III) containing more than one ligand exist.[2]

A recent study [3] showed that the ferrocenium ion is able to form stable yellow complexes with a variety of organic ligands.

Experimental.—A stock solution of ferrocenium perchlorate was prepared by electrolytic oxidation of ferrocene in ethanol, methanol, and acetone containing perchloric acid.[4] The concentration of the ferricenium perchlorate in ethanol was adjusted so that when it was added to the other solvent the amount of ethanol in the resulting solution made no difference to the spectra of the solution. Solutions of thiocyanate were made from "AnalaR" ammonium thiocyanate in the appropriate solvent. The water content of the solutions was adjusted by adding weighed amounts of water to the organic solvent.

The acetone used was redistilled and dried over potassium carbonate. Redistilled methanol was distilled from magnesium turnings. Absolute alcohol was used without further purification. Dimethylformamide was purified by distillation. "AnalaR" glacial acetic acid was used as such.

Spectra were taken with a Hilger Uvispek spectrophotometer with a glass prism and glass cells.

Results and Discussion.—The absorption spectrum of an ethanolic ferrocenium solution containing an excess of thiocyanate (Fig. 1) illustrates the effect of water. The stoicheiometry in ethanol solution, investigated by Job's method [5] (Fig. 2), indicates a 1 : 1 compound. Similar plots indicate that a 1 : 1 compound is formed also in all the other solvents mentioned. The absorption of the ferrocenium thiocyanate is dependent on the nature of the solvent, as shown by Fig. 3.

Adding water to methanol, ethanol, and acetone solutions of ferrocenium thiocyanate

[1] Baldwin and Svirbely, *J. Amer. Chem. Soc.*, 1949, **71**, 3326.
[2] Lister and Rivington, *Canad. J. Chem.*, 1955, **33**, 1572.
[3] Smith, *J. Inorg. Nuclear Chem.*, 1960, **14**, 290.
[4] Page and Wilkinson, *J. Amer. Chem. Soc.*, 1952, **74**, 6149.
[5] Job, *Ann. Chim.* (*France*), 1928, **9**, 113.

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decreases the intensity of absorption. The effect of the added water may be expressed in terms of the equilibrium constant $K^n_{solvent}$ where

$$K^n_{solvent} = \frac{\gamma(C_5H_5)_2FeSCN}{\gamma(C_5H_5)_2Fe^+ . \gamma CNS^-} \cdot \frac{\gamma^n H_2O}{\gamma_{solvent}} \cdot \frac{[(C_5H_5)_2FeSCN][H_2O]^n}{[(C_5H_5)_2Fe^+][CNS^-][solvent]}$$

and γ denotes an activity coefficient. First, for acetone–water mixtures, wavelengths were chosen at which Beer's law held for ferrocenium thiocyanate in pure acetone solution. Then, on the assumption that the molar extinction coefficient of the compound remained constant on addition of water and with wavelengths where the absorption of the free ferrocenium ion could be neglected, the concentration of the ferrocenium thiocyanate was estimated.

The values obtained for the concentration quotient $K'_{acetone}$ for various additions of water are shown by Table 1 for $n = 1$. The values of the activity coefficients of the

TABLE 1.

$(C_5H_5)_2FeSCN$ (10^{-4}M)	$(C_5H_5)_2Fe^+$ (10^{-4}M)	NH_4CNS (10^{-2}M)	H_2O (M)	Acetone (M)	$K'_{acetone}$	$\frac{\gamma_{H_2O}}{\gamma_{acetone}} . K_{acetone}$
0·765	0·235	1·000	2·78	13·4	67·5	—
0·495	0·506	1·000	8·34	12·0	67·9	81·0
0·408	0·592	1·000	11·12	11·3	67·9	77·3
0·325	0·675	1·000	13·9	10·4	64·2	69·0

compound and the ionic species under the varying solvent conditions are not known. However, the activites of the water in acetone and of acetone in water at the higher mole fractions of water may be determined from vapour-pressure data,[6] and the influence of the

FIG. 1. *Absorption spectra* (1 *cm. cell*) *of* 2·00 × 10^{-4}M-*ferrocenium thiocyanate in ethanol containing* (1) 0, (2) 2·78, (3) 5·56, (4) 13·9, *and* (5) 27·8 *mol. of water.*

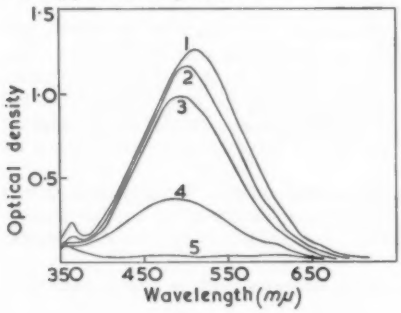
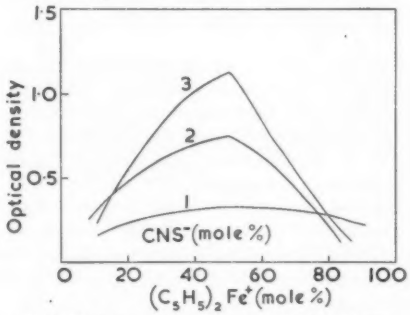


FIG. 2. *Continuous-variation plot for ferrocenium thiocyanate in ethanol* (1 *cm. cell*).



(1) λ 450 mμ. (2) λ 500 mμ. (3) λ 550 mμ.

variation of the appropriate activites of the solvent system on $K'_{acetone}$ is detailed by Table 1. Under the varying solvent conditions the activites of the ionic species and of the complex will change, especially in the region of low mole fractions of water.

Similar considerations resulting from the spectra of water–ethanol and water–methanol solutions of ferrocenium thiocyanate may be expressed in terms of the equilibrium constants $K^n_{ethanol}$ and $K^n_{methanol}$. Again, the values of the activity coefficients of the compound and of the ionic species under the solvent conditions are not known. However, the values of the activity coefficients of water in alcohols and of the alcohols in water at the mole fractions concerned here have been determined by Butler *et al.*[7] The values of the concentration quotients $K^{1\prime}_{ethanol}$ and $K^{2\prime}_{ethanol}$ are shown in Table 2, as well as the

[6] International Critical Tables, Vol. III, p. 290, 1928.
[7] Butler, Thomson, and MacLennan, 1933, 674.

effect of the activity coefficients. The results for water–methanol system are shown in Table 3.

In the three solvent systems the activity coefficients of the solvent mixtures considerably affect the values of the concentration quotients, and variations resulting from the changing activity coefficients of the ionic species also occur. In each case the essential

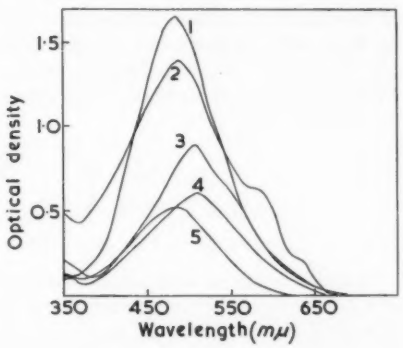


FIG. 3. *Absorption spectra of* $1{\cdot}00 \times 10^{-4}$M-*ferrocenium thiocyanate in* (1) *acetone,* (2) *acetic acid,* (3) *methanol,* (4) *ethanol, and* (5) *dimethylformamide* (1 *cm. cell*).

process involved in the dissociation of the compound is replacement of the thiocyanate ion by a water molecule. However, from the results it is impossible to elucidate the solvation of the organic molecules. For alcohol–water systems consistent results for the final

TABLE 2.

$(C_5H_5)_2FeSCN$ (10^{-4}M)	$(C_5H_5)_2Fe^+$ (10^{-4}M)	NH_4CNS (10^{-3}M)	H_2O (M)	EtOH (M)	$K^{1\prime}_{EtOH}$	$K^{2\prime}_{EtOH}$	$\frac{\gamma^2_{H_2O}}{\gamma_{MeOH}} \cdot K^{2\prime}_{EtOH}$
1·60	0·40	2·00	2·78	16·27	34·2	190	878
1·29	0·71	2·00	5·58	15·40	32·8	360	1150
0·94	1·06	2·00	8·34	14·25	25·9	384	944
0·45	1·55	2·00	13·9	12·80	15·6	438	701

TABLE 3.

$(C_5H_5)_2FeSCN$ (10^{-4}M)	$(C_5H_5)_2Fe^+$ (10^{-4}M)	NH_4CNS (10M)	H_2O (M)	MeOH (M)	$K^{1\prime}_{MeOH}$	$K^{2\prime}_{MeOH}$	$\frac{\gamma^2_{H_2O}}{\gamma_{MeOH}} \cdot K^{2\prime}_{MeOH}$
0·875	0·125	1·00	2·78	23·63	82·5	225	527
0·713	0·287	1·00	5·56	22·4	61·7	346	678
0·400	0·600	1·00	10·15	19·9	34·0	345	569
0·250	0·750	1·00	13·9	18·7	24·8	345	497

product in Tables 2 and 3 are obtained when $n = 2$. Bearing in mind the uncertainties of the state of solvation of the species in these solutions the following equilibrium process is tentatively proposed for the water–alcohol solutions:

$$(C_5H_5)_2Fe^+(H_2O)_2 + CNS^- + ROH \rightleftharpoons (C_5H_5)_2FeSCN,ROH + 2H_2O$$

The spectrophotometric data indicate that the maximum absorption in the solvents containing the C=O group is in the region 490 mμ whilst the maximum absorption in the alcohols occurs in the region 510 mμ which may be due to structural differences in these solvents.[8]

ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY,
GLASGOW, C.1.

[*Received, June 8th,* 1960.]

[8] Chu, Fujii, and Li, *J. Amer. Chem. Soc.*, 1955, **77**, 2085.

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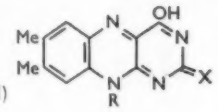
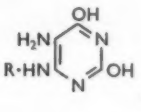
89. *Pteridine Derivatives. Part VIII.*[1] *A New Synthesis of Riboflavin and Related Isoalloxazines.*

By R. M. Cresswell, Thomas Neilson, and H. C. S. Wood.

The synthesis of alloxazines by condensation of 4,5-diaminopyrimidines with the dimer of 3,4-dimethyl-*o*-benzoquinone has recently been described by Bardos, Olsen, and Enkoji.[2] In Part VII [1] of this series we described the synthesis of "lumiflavin 2-imine" (I; R = Me, X = NH) by a modification of this method. We have now extended the reaction to the synthesis of riboflavin and related isoalloxazines.


(I)


(II)

Condensation of 5-amino-4-D-ribitylaminouracil (II; R = D-ribityl) with the dimer [2] of 3,4-dimethyl-*o*-benzoquinone gave a 29% yield of riboflavin (I; R = D-ribityl, X = O), identified by mixed m. p., paper chromatography, and ultraviolet and infrared spectra. The pyrimidines (II; R = Me, $CH_2 \cdot CH_2 \cdot OH$, D-mannityl, and D-sorbityl) similarly gave the corresponding isoalloxazines (I). The 5-aminopyrimidines (II) were prepared by reduction of the 5-nitro-compounds [3,4] with sodium dithionite.

Lumiflavin (I; R = Me, X = O) and its 2-hydroxyethyl analogue were identified by comparison with authentic materials.[5,6] The D-sorbityl compound agrees in m. p. and optical rotation with that recorded by Euler *et al.*[7] although these authors do not give preparative or analytical details.

Experimental.—For general instructions see Part VII.[1]

Riboflavin (I; R = D-Ribityl, X = O). 5-Nitro-4-D-ribitylaminouracil [3] (0·25 g.) in water (10 c.c.) at 90° was treated with N-sodium hydroxide (5 c.c.), followed by sodium dithionite portionwise until the solution became colourless. Glacial acetic acid was added to the cooled solution to give pH 4, followed by dimeric 3,4-dimethyl-*o*-benzoquinone [2] (0·15 g.) in ethanol (10 c.c.). The mixture was heated for 30 min. on the steam-bath and finally acidified by 12N-hydrochloric acid. On cooling, riboflavin separated as orange needles (0·09 g., 29%), m. p. 288° (lit.,[8] 292°), $[\alpha]_D^{23}$ −116° (*c* 0·53 in 0·1N-NaOH) (lit.,[9] −115°). The ultraviolet and infrared spectra were identical with those of an authentic sample.

The following isoalloxazines (orange needles) were prepared by similar methods, and where applicable the ultraviolet and infrared spectra of the products were compared with those of authentic materials: Lumiflavin (I; R = Me, X = O) (obtained from 4-methylamino-5-nitrouracil [3] in 40% yield), m. p. 325—326° (lit.,[5] 328°).

9-2′-Hydroxyethyl-6,7-dimethylisoalloxazine (I; R = $CH_2 \cdot CH_2 \cdot OH$, X = O) (from 4-2′-hydroxyethylamino-5-nitrouracil; [3] 29%), m. p. 297—299° (lit.,[6] 300—301°).

9-D-*Mannityl*-6,7-*dimethylisoalloxazine* (I; R = D-mannityl, X = O) (from 4-D-mannitylamino-5-nitrouracil; [4] 49%), m. p. 285° (Found: C, 52·4; H, 5·2; N, 13·5. $C_{18}H_{22}N_4O_7,0{\cdot}5H_2O$ requires C, 52·1; H, 5·6; N, 13·5%), $[\alpha]_D$ +61° (*c* 0·18 in 0·05N-NaOH), $\lambda_{max.}$ 223 (ε 34,300), 266 (ε 37,000), 374 (ε 12,600), and 444 mμ (ε 13,500) at pH 1, 222 (ε 23,000), 270 (ε 26,700), 356 (ε 8900), and 445 mμ (ε 8500) at pH 13.

[1] Part VII, Cresswell, Hill, and Wood, *J.*, 1959, 698.
[2] Bardos, Olsen, and Enkoji, *J. Amer. Chem. Soc.*, 1957, **79**, 4704.
[3] Cresswell and Wood, *J.*, 1960, 4768.
[4] Cresswell, Neilson, and Wood, *J.*, 1960, 4776.
[5] Kuhn, Rudy, and Wagner-Jauregg, *Ber.*, 1933, **66**, 1950.
[6] Fall and Petering, *J. Amer. Chem. Soc.*, 1956, **78**, 377.
[7] Euler, Karrer, Malmberg, Schöpp, Benz, Becker, and Frei, *Helv. Chim. Acta*, 1935, **18**, 522.
[8] Kuhn, Reinemund, Weygand, and Ströbele, *Ber.*, 1935, **68**, 1765.
[9] Kuhn and Rudy, *Ber.*, 1935, **68**, 169.

6,7-*Dimethyl*-9-D-*sorbitylisoalloxazine* (I; R = D-sorbityl, X = O) (from 5-nitro-4-D-sorbitylaminouracil;[4] 23%), m. p. 275° (lit.,[7] 272°) (Found: C, 52·1; H, 5·5; N, 13·4. $C_{18}H_{22}N_4O_7,0{\cdot}5H_2O$ requires C, 52·1; H, 5·6; N, 13·5%), $[\alpha]_D$ −45° (*c* 0·18 in 0·05N-NaOH) (lit.,[7] −47·7°), $\lambda_{max.}$ 222 (ε 27,500), 266 (ε 29,600), 374 (ε 10,000), and 444 (ε 11,400) at pH 1, 222 (ε 25,000), 270 (ε 28,100), 356 (ε 9900), and 449 mμ (ε 9700) at pH 13. With pyridine andacetic anhydride it gave the *acetate*, m. p. 238° (lit.,[7] 237°) (Found: C, 54·5; H, 5·9. $C_{28}H_{32}N_4O_{12},C_2H_5{\cdot}OH$ requires C, 54·4; H, 5·8%).

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THE ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY,
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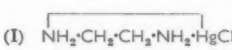
90. *The Infrared Spectra and Structures of the Complexes Dichloro(ethylenediamine)-zinc, -cadmium, and -mercury.*

By G. NEWMAN and D. B. POWELL.

THE usual complexes of zinc(II) and cadmium(II) with ethylenediamine contain 2 or 3 chelated ligands, such as $[Cd\ en_3]Cl_2$.* Insoluble compounds have been prepared of the type $M\ enCl_2$ (M = Zn, Cd, Hg), by addition of ethylenediamine to solutions of the respective chlorides. It has been suggested [1] that the mercury complex contains a chelated ethylenediamine group, as in (I). This is supported by Sutton's ultraviolet spectroscopic measurements.[2]



(I) $NH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2{\cdot}HgCl_2$ $\qquad$ $(C_2H_4)PtCl_2{\cdot}NH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2{\cdot}PtCl_2(C_2H_4)$ (II)

The infrared spectra of these compounds (Figs. 1*b*, 1*c*, 1*d*) are much simpler than that of the chelated $[Cd\ en_3]Cl_2$ (Fig. 1*a*), and very similar to that of compound (II) (Fig. 1*e*) when allowance is made for the absorption peaks due to ethylene. Compound (II) contains a bridging ethylenediamine group with the *trans*-configuration, and a fairly complete assignment of the absorption bands to the fundamental vibrations has been made on this basis.[3]

In the Table the absorption frequencies for dichloro(ethylenediamine)-zinc, -cadmium, and -mercury are compared with those obtained for the platinum compound (II). In spite of some quite large frequency changes, the corresponding absorption bands can be

Infrared absorption frequencies (cm.$^{-1}$) of ethylenediamine complexes.

Zn $enCl_2$	Cd $enCl_2$	Hg $enCl_2$	(II)	Assignment
1575	1612	1610	1551	δNH_2 scissors
1455	1483	1490	1452	δCH_2 scissors
1377	1374?	1374?	1375	δCH_2 wag
1339	1334	1351	1336	δNH_2 wag
1278	1278	1278	1280	δCH_2 twist
1140	1099	1180	1190	δNH_2 twist
1008	1017	1007	1052?	ν skeletal
792	847	820	752	δCH_2 rock
665 (630)	540	683	653	δNH_2 rock

readily identified, and there seems no doubt that the ethylenediamine group in all these compounds has the same configuration. An interesting feature of the spectra (1*b*, *c*, and

* The symbol en represents the ethylenediamine molecule.

[1] O'Brien, *J. Amer. Chem. Soc.*, 1948, **70**, 2771.
[2] Sutton, *Austral. J. Chem.*, 1959, **12**, 637.
[3] Powell and Sheppard, *J.*, 1959, 3089.

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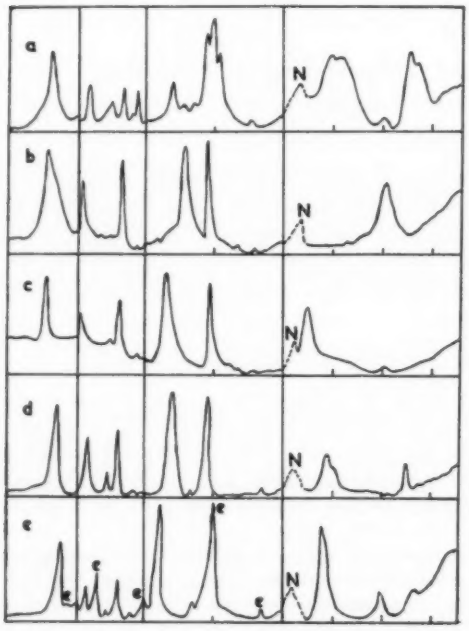
d) is the prominence of the skeletal stretching vibration near 1000 cm.$^{-1}$. This vibration was difficult to detect in the spectrum of compound (II), and is obscured by the strong absorption in this region due to the ethylene group.

Chelate structures for dichloro(ethylenediamine)-zinc, -cadium, and -mercury would clearly be inconsistent with this infrared evidence, and the most probable structures would be polymeric chains with ethylenediamine molecules joined to different metal atoms, *viz.*,

. . . $HgCl_2$ enHgCl enHgCl_2 en . . .

Such a structure has been found [4,5] for the dioxan–mercuric chloride complex, $Hg(C_4H_8O_2)Cl_2$, and would account for the insolubility of these compounds. With the



Infrared absorption spectra of complexes:
a, $[Cd\ en_3]Cl_2$; b, Cd $enCl_2$; c, Zn $enCl_2$; d, Hg $enCl_2$; *and* e, (II).
(1) 1750—1500 and 1250—400 cm.$^{-1}$, Nujol mulls; 1500—1250 cm.$^{-1}$, hexachlorobutadiene mull.
(2) Absorption marked N is due to Nujol; absorption peaks marked "e" in 1(e) are due to ethylene.

cadmium chloride complex, the low, variable values obtained for the C, H, and N determinations probably arise from the formation of chains of fairly low molecular weight and terminated by $CdCl_2$ groups. The infrared spectrum of another known [1] mercuric chloride complex, $(HgCl_2)_2$ en, also has a *trans*-bridging ethylenediamine group. This compound with the ethylenediamine group bridging two mercuric chloride molecules would probably represent the first stage in the building of the polymeric chain, which reaches the limiting case with the compound Hg $enCl_2$.

Experimental.—All spectra were obtained with a Hilger H.800 spectrometer with rock-salt and potassium bromide optics. The samples were examined as dispersions in liquid paraffin and hexachlorobutadiene.

Hg $enCl_2$ and $(HgCl_2)_2$en were prepared by O'Brien's method.[1] Cd en Cl_2 was prepared in the same manner as its mercury analogue; aqueous ethylenediamine (*ca.* 1M) was added to

[4] Tarte and Laurent, *Bull. Soc. chim. France*, 1957, 403.
[5] Hassel and Hvoslef, *Acta Chem. Scand.*, 1954, **8**, 1953.

aqueous 1M-cadmium chloride, giving a white insoluble precipitate, which was washed successively with water, alcohol, and ether, and dried *in vacuo* (P_2O_5) (Found: C, 9·1, 8·8; H, 3·2, 3·0; N, 10·5. Cd $enCl_2$ requires C, 9·9; H, 3·3; N, 11·5%). Zn $enCl_2$ can be obtained as a white precipitate, on addition of 1 mole of ethylenediamine in 20% aqueous alcohol (v/v) to an alcoholic solution containing 1 mole of anhydrous zinc chloride (Found: C, 11·9; H, 4·2. Zn $enCl_2$ requires C, 12·2; H, 4·1%).

Difficulty was experienced in repeating the last preparation and conditions appear to be critical for the formation of this complex. In the spectrum shown (Fig. 1*d*) the shoulder at 630 cm.$^{-1}$ may be due to impurity, as its intensity varied with different preparations, and was decreased by repeated washing with water.

One of the authors (G. N.) thanks the Department of Scientific and Industrial Research for a maintenance grant.

Sir John Cass College, Jewry St., London, E.C.3. [*Received, June 15th*, 1960.]

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91. *The Action of* N-*Bromosuccinimide on* 1,2,3,4-*Tetraphenylcyclobutane.*

By W. Baker, (Miss) J. W. Hilpern, and J. F. W. McOmie.

In an attempt to introduce one or two double bonds into the four-membered ring of 1,2,3,4-tetraphenylcyclobutane, a solution of this compound in carbon tetrachloride was treated with *N*-bromosuccinimide. The product was shown to be 1,2,3,4-tetraphenylbuta-1,3-diene, presumably formed by bromination followed by dehydrobromination with concurrent ring-opening.

The tetraphenylcyclobutane was prepared in 20% yield by ultraviolet irradiation of stilbene. Previously this compound had been made in low yield by exposure of stilbene to sunlight [1] for 2 years and in 7% yield by using ultraviolet light.[2] The cyclobutane is known to have the *cis-anti-cis*-structure.[3]

Experimental.—*1,2,3,4-Tetraphenylcyclobutane.* Stilbene (20 g.) in warm benzene (150 ml.) was irradiated in an atmosphere of nitrogen for 48 hr. in an annular Pyrex glass vessel (5·5 cm. internal diameter) surrounding a Hanovia U.V.S. 500 ultraviolet lamp. After evaporation of the solvent, the residue was shaken with ether and filtered. The insoluble portion was crystallised four times from ethanol, giving 1,2,3,4-tetraphenylcyclobutane (4 g.), m. p. 162—163° (lit., 163°). Stilbene (3 g.) was obtained from the ether extract.

1,2,3,4-Tetraphenylbuta-1,3-diene. A mixture of the cyclobutane (1 g.), *N*-bromosuccinimide (0·4 g.), dibenzoyl peroxide (40 mg.), and carbon tetrachloride was boiled gently under reflux for 1 hr. After being filtered the solution was evaporated under reduced pressure and the residue purified by chromatography on alumina with benzene as solvent. The material which formed a yellow band (violet under ultraviolet light) was eluted with benzene and purified by four-fold crystallisation from benzene, giving 1,2,3,4-tetraphenylbuta-1,3-diene (0·4 g., 40%), m. p. and mixed m. p. with an authentic [4] specimen, 183—184° (Found: C, 93·9; H, 6·5. Calc. for $C_{28}H_{22}$: C, 93·8; H, 6·2%). The infrared spectrum of the product was identical with that of a sample kindly supplied by Professor J. Coops.

The University, Bristol. [*Received, June 24th*, 1960.]

[1] Ciamician and Silber, *Ber.*, 1902, **35**, 4128.
[2] Pailer and Müller, *Monatsh.*, 1948, **79**, 615.
[3] Dunitz, *Acta Cryst.*, 1949, **2**, 1.
[4] Coops, Hoijtink, Kramer and Faber, *Rec. Trav. chim.*, 1953, **72**, 765.

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92. *Submicro-methods for the Analysis of Organic Compounds Part XIII.* The Cryoscopic Determination of Molecular Weight.*

By R. Belcher, M. Sobotka, and W. I. Stephen.

The cryoscopic method for the determination of molecular weight [1] appeared to be very suitable for adaption to the submicro-scale because of the favourable depression of the melting point of camphor, the solvent which is generally used. Because of the small quantities involved it is necessary to use capillaries instead of the comparatively wide tubes used on the microscale and the main problem was the weighing and transference of the sample without loss to the weighed camphor. This was overcome by weighing the capillary, transferring the camphor to it and reweighing the added camphor on the *micro-balance*. To transfer the sample quantitatively after weighing on the *submicro-balance*, a new technique described in the experimental section was developed. This has certain limitations but has proved satisfactory for a wide range of organic compounds.

Several methods of heating the capillary were examined, including the use of a conventional oil-bath, but in this medium it was not only difficult to make accurate observations of the melting and crystallising points of the solution in the narrow tube, but also the tube could not be shaken. The preferred method makes use of a commercial electrical melting-point apparatus, which provides adequate magnification of the tube and its contents; moreover, the possibility of moving the tube in the apparatus enables the solute to be thoroughly mixed with solvent during the melting process.

Since the method involves temperature differences only, this type of apparatus can be used provided that the rates of heating and cooling at temperatures in the immediate vicinity of the melting and crystallising point are controlled. In the present work, the crystallisation temperature was found to be more easily observed than the melting point and therefore was used throughout the study. Observations of the crystallisation of pure camphor indicated that the rate of cooling of the apparatus was very critical. When the temperature of the heating block was raised to 5° above the melting point of camphor, *i.e.*, to about 185°, and the current to the heating element was then cut off, so that a rapid cooling rate was established, the characteristic fine network of camphor crystals appeared at 180°. However, when the cooling rate was adjusted by rheostat control so that the temperature fell 1° per minute, crystallisation occurred at 176°. An intermediate cooling rate of 1° per 20 seconds gave a crystallisation point of 178·4—178·6°. This rate of cooling was sufficiently slow to allow observation of the crystallisation temperature to be made within 0·2°. Similar differences in temperature were observed for the crystallisation points of a solution of acetanilide in camphor so that the actual depression of the crystallisation point of camphor was constant for a particular rate of cooling.

Determination of the cryoscopic constant of camphor by using acetanilide as solute gave values for 36 to 40, depending on the cooling rate. When this was standardised during any one series of determinations the molecular depression remained constant.

In preliminary experiments the capillaries were made with rounded ends. A series of qualitative tests with acetanilide as solute gave abnormal but constant values for the crystallisation temperature. These were attributed to the formation of eutectic mixtures of acetanilide and camphor, and true solutions were not obtained. When flat-ended tubes were used and agitated in the apparatus, the loosened platinum wire acted as a stirrer and the contents of the tube were adequately mixed. This completely prevented the formation of the low-melting eutectics and was adopted in all the quantitative work.

* Part XII, *J.*, 1960, 3830.

[1] Le Fèvre, *Nature*, 1930, **126**, 760; Le Fèvre and Tideman, *Nature*, 1931, **127**, 972; Le Fèvre and Webb, *J.*, 1931, 1211; Le Fèvre and Tideman, *J.*, 1931, 1729.

Results for a number of organic compounds are given in the Table. The weights of sample ranged from 30 to 96 μg., dissolved in sufficient camphor to give solutions of 0·2—0·3M-concentration. Camphor was the only solvent examined in the present work, but it is reasonable to suppose that the method can be applied with other solvent systems.[2]

The procedure which has been developed for weighing the sample can only be used with solid organic compounds which melt without decomposition. Many organic compounds sublime without melting when heated, but a sufficient weight of sublimate can be collected on the sampling wire when the end of the wire is held over the heated compound. More care is then necessary in handling the wire, especially when the sublimate is light and bulky.

Experimental.—Apparatus. Gallenkamp electrically heated melting-point apparatus, single melting-point tube type.

Anschutz thermometer, 145—205° range. Gas-heated aluminium block with 0—360° thermometer.

Capillary tubes, approximately 50 mm. long, of 2 mm. internal-diameter at the open end, tapering to 0·5—0·6 mm. at the sealed end. Drawn from *clean*, hard glass tubing.

Platinum cup. A depression of about 3 mm. diameter, and 2 mm. depth is made in the centre of a 10 mm. square of thin platinum sheet. A handle of platinum wire is welded on.

Reagent: Camphor (microanalytical reagent grade).

Determination of cryoscopic constant of camphor. A submicro-capillary tube is charged with about 1 mg. of camphor by Pregl's technique [3] for inserting the camphor into the bottom of the tube. A 15 mm. length of platinum wire (0·03 mm. diam.) is added and the tube is sealed about 2 mm. above the wire by means of a very fine flame from an oxy-coal gas hand-torch. Another tube, but of known weight, is similarly charged with camphor and is reweighed on a microbalance. A crystal of acetanilide is put into a small platinum cup placed on an aluminium heating block. The acetanilide is heated to slightly above its m. p. and one end of another similar piece of platinum wire whose weight has been determined by means of the submicro-balance is touched against the molten substance and then immediately withdrawn. The weight of substance adhering to the tip of the wire is found by reweighing the wire. The wire is placed sample-end first in the capillary which is sealed off as before.

The capillary containing camphor alone is placed in the m. p. apparatus previously heated to 175°. Heating is continued until a temperature 5° above the m. p. is reached. The current to the heating element is reduced to a value which gives a cooling rate of approx. 1° per 20 sec., and the temperature at which the first crystals appear in the clear melt is read to 0·1°. The camphor is again melted and cooled, the process being repeated three times. The crystallisation temperature should be reproducible to ±0·1°. A similar procedure is applied to the tube containing the acetanilide, after the temperature of the apparatus has been allowed to drop to about 160°, but during the melting process the tube is raised and rotated in the apparatus, so that the platinum wire moves about in the tube and mixes the contents thoroughly.

Determination of molecular weights of organic compounds. The procedure described above was repeated with other organic compounds which can be melted without decomposition (see Table).

Substance *	Molecular weight Theory	Found	Substance *	Molecular weight Theory	Found
8-Hydroxyquinoline	145·2	144, 149, 148, 144	Phenacetin	179·2	183
Benzoic acid	122·1	119, 127, 124	Acetanilide	135·2	134
Cinnamic acid	148·2	142	*p*-Chlorobenzoic acid	156·7	155
Sulphonal	228·3	235	Hippuric acid †	179·2	167
p-Nitroaniline	138·1	132	Trifluoroacetanilide	189·1	186
m-Dinitrobenzene	168·1	172	2,2′-Bistrifluoromethylazobenzene	318	307

* All were of Microanalytical Standard Grade except the last.
† This substance appeared to decompose during the determination.

[2] Pirsch, *Angew. Chem.*, 1938, **51**, 73.
[3] Pregl, "Die Quantitative Organische Mikroanalyse," 3rd edn., Springer Verlag, Berlin, 1930.

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We are indebted to Mr. P. Gouverneur, Royal Dutch Shell Co., Amsterdam, for independently checking the procedure. One of us (M. S.) thanks the British Council for financial support.

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93. NN'-*Di*(*cyclohepta*-2,4,6-*trienyl*)*urea*, alias *Tropylium Isocyanate*.

By W. VON E. DOERING and L. E. HELGEN.

DEWAR and PETTIT achieved an elegant, generally applicable synthesis of the tropylium ion in 1955 by a Curtius reaction with cyclohepta-2,4,6-trienecarboxylic acid (norcaradienecarboxylic acid).[1,2,3] Two intermediates were isolated. One, a liquid, was formulated as the covalent isocyanatonorcaradiene and synthesized independently by *rapid* addition of an excess of aqueous sodium cyanate to aqueous tropylium fluoroborate.[3] The other was water-insoluble, high-melting, crystalline, and, it was asserted, isomeric with the former, and it was formulated as the salt-like tropylium isocyanate: it was synthesized by *slow* addition of aqueous sodium cyanate to aqueous tropylium fluoroborate. Both products were transformed into tropylium bromide on treatment with hydrogen bromide.[2]

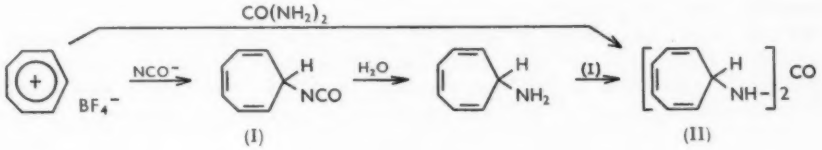
Of less importance than the synthesis of tropylium ion itself, the disclosure of a pair of valency tautomers related as covalent and ionic isomers was nonetheless striking, the more so because the two isomers appeared capable of indefinite existence, either alone or in contact with each other. Since a closed system composed of a liquid and a solid isomer can be at equilibrium at a given pressure at only one temperature, it is clear that the two isomers are *not* in equilibrium. However, the synthesis of both of them under essentially identical conditions from an aqueous solution of tropylium fluoroborate and sodium cyanate demands the establishment of equilibrium in water. The probability of satisfying these conditions seemed sufficiently small to call into question the structure and, thereby, the number of the components in the system.

The structure, isocyanatonorcaradiene (cyclohepta-2,4,6-triene isocyanate [4]), assigned to the liquid isomer is corroborated by the finding of a nuclear magnetic resonance spectrum very similar to that of methyl cyclohepta-2,4,6-trienecarboxylate [4] and a very strong infrared band at 4·4 μ.[5]

However, the structure of tropylium isocyanate assigned to the solid is incorrect. Elemental analysis is in better accord with the formula $C_{15}H_{16}N_2O$ than with C_8H_7NO. The ultraviolet spectrum $\lambda_{max.}$ 256 (log ε 3·9) and $\lambda_{min.}$ 222 mμ (log ε 3·5) is in better accord with that of cycloheptatriene (tropilidene) [6] than with that of the tropylium ion.[7] The infrared spectrum shows no absorption at 4·63 μ characteristic of the cyanate ion. An independent synthesis of the solid was effected by mixing an aqueous solution of tropylium

[1] Dewar and Pettit, *Chem. and Ind.*, 1955, 199.
[2] Dewar and Pettit, *J.*, 1956, 2021.
[3] Dewar and Pettit, *J.*, 1956, 2026.
[4] Doering, Laber, Vanderwahl, Chamberlain, and Williams, *J. Amer. Chem. Soc.*, 1956, **78**, 5448.
[5] Davison, *J.*, 1958, 3712.
[6] Doering and Knox, *J. Amer. Chem. Soc.*, 1953, **75**, 297.
[7] Doering and Knox, *J. Amer. Chem. Soc.*, 1954, **76**, 3203.

bromide and urea.[8] Its m. p. and infrared spectrum were identical with those of the product prepared by Dewar and Pettit's method from tropylium bromide or fluoroborate and potassium cyanate shows the substance to be a ditropylurea. A tentative decision between the symmetrical and the unsymmetrical formulation is based on the feeling that Dewar and Pettit's reaction would most probably lead to the symmetrical derivative. Irrespective of whether addition of the aqueous sodium cyanate is gradual or rapid, the



initial product is the isocyanate (I). During the gradual addition there is ample opportunity for this to be hydrolysed to the still unknown aminocycloheptatriene *via* the carbamic acid and this with unchanged isocyanate (I) then leads to the symmetrical urea.

Correction of this structure leads to a few minor revisions in Dewar and Pettit's work. The formation of the urea in the Curtius reaction must have depended on the presence of variable amounts of water. In this connection, the observation that " the individual yields of the solid isomer varied from 0% to 50% " is relevant.[2] Conversion of the urea into tropylium bromide by hydrogen bromide should doubtless be reformulated as an example of the general reaction of *N*-cycloheptatrienyl amides with hydrogen bromide.[8] Discussion of valency tautomerism in this series becomes superfluous.

Experimental.—NN'-*Di*(*cyclohepta*-2,4,6-*trienyl*)*urea*. (*a*) As recorded by Dewar and Pettit,[3] potassium cyanate (0·34 g.) in water (10 g.) was added dropwise in 10 min. to a stirred solution of tropylium bromide (1·00 g.) in water (10 g.). When the addition was about half-complete, crystals began to appear. After being stirred for 3 hr., the mixture was filtered to yield colourless crystals of the *urea*, m. p. 186·5—188·0° (0·23 g., 46%). Four recrystallizations from ethyl acetate raised the m. p. to 190—191° (Found: C, 74·8; H, 6·9; N, 11·6. $C_{15}H_{16}N_2O$ requires C, 75·0; H, 6·7; N, 11·7%).

(*b*) Reaction with tropylium fluoroborate in place of the bromide gave the same product, m. p. and mixed m. p. 190—191° (Found: C, 75·0; H, 7·0; N, 11·8%).

(*c*) No visible change followed the addition of urea (0·18 g.) in water (3 g.) to a stirred solution of tropylium bromide (1·01 g.) in water (10 g.) until further addition of sodium hydrogen carbonate (0·49 g.) in water (5 g.). After an immediate precipitation, evolution of gas, and decolorisation, the mixture was stirred for 3 hr. and filtered to yield the urea, m. p. and mixed m. p. 189—190° (after one recrystallization from ethyl acetate). The infrared spectra of all these samples were superimposable.

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[8] Doering and Knox, *J. Amer. Chem. Soc.*, 1957, **79**, 4127.

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94. *Supinine from the Seeds of* Trichodesma zeylanicum, *R.Br.*

By J. O'Kelly and K. Sargeant.

The alkaloid supinine, the pharmacology of which is at present of interest in Australia as the probable causative agent in the heliotrope poisoning of sheep,[1,2] has previously been obtained in low yields from *Heliotropium supinum*, L., *Heliotropium europaeum*, L., and *Tournefortia sarmentosa*, Lam.[3]

We now report its isolation, in about 1% yield, from the dried seeds of *Trichodesma zeylanicum*. These seeds were collected in Tanganyika where the plant is a common weed. They contain in all about 2% of basic material. Paper chromatography in a variety of solvent systems suggests that this basic material is almost entirely supinine although at least two other bases are present in minor quantities.

Only small amounts of alkaloidal *N*-oxides occur in the seeds. This was shown by the very small increase in the content of chloroform-soluble bases after the reduction of a chloroform-insoluble basic extract with zinc dust and sulphuric acid.

Experimental.—Finely ground *Trichodesma zeylanicum* seeds (740 g.) were extracted with absolute alcohol in a Soxhlet apparatus for 8 hr. (12 changes). The extract (1200 ml.), after dilution with water (400 ml.), was made acidic to Congo Red paper with citric acid, concentrated to 200 ml. under reduced pressure, exhaustively extracted with ether and chloroform, and basified with an excess of sodium carbonate, and the total bases (15·3 g.) were extracted with chloroform. Crystallisation from ethyl acetate gave colourless needles (7·0 g.), m. p. 138—142°, which, after several recrystallisations from ethyl acetate and finally methanol, had m. p. 147—148·5°, $[\alpha]_D^{21}$ −13·4° (*c* 2·4 in EtOH) (Found: C, 63·4, 63·3; H, 8·9, 8·9; N, 5·1, 5·2. Calc. for $C_{15}H_{25}NO_4$: C, 63·6; H, 8·9; N, 4·9%). This product was shown to be supinine, by a mixed m. p. determination and by comparison of infrared absorption spectra.

Paper chromatography of the crude bases in butan-1-ol–acetic acid–water,[2] with potassium iodobismuthate in acetic acid as the spray reagent,[4] showed the presence of at least three constituents. The major one had R_F 0·34. The two others had R_F 0·04, and 0·63 respectively and were present in very much smaller amounts. The major spot, which had the same R_F value as pure supinine, was not resolved in the following solvent systems: (1) butan-1-ol–hydrochloric acid–water on paper impregnated with potassium chloride; [4] (2) cyclohexane–diethylamine on paper impregnated with formamide; [5] (3) butan-1-ol–citric acid–water on paper impregnated with sodium dihydrogen citrate.[6]

The sodium carbonate solution left after the removal of the bases was acidified to 2N with sulphuric acid. The resultant solution was stirred with zinc dust for 24 hr., basified with sodium carbonate, and extracted with chloroform. The gum obtained (0·5 g.), when submitted to paper chromatography in butan-1-ol–acetic acid–water, appeared to have approximately the same composition as the mixture of bases already examined.

Thanks are offered to Dr. W. D. Raymond who kindly supplied the plant material, and to Mrs. H. C. Crowley and Dr. C. C. J. Culvenor who provided a sample of supinine isolated from *Heliotropium supinum*.

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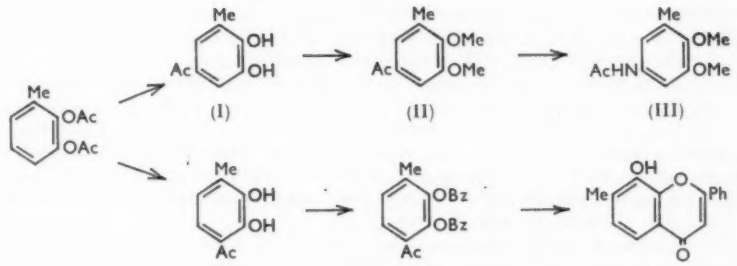
56/62, Gray's Inn Road, London, W.C.1. [*Received, August 12th,* 1960.]

[1] Bull, Dick, Keast, and Edgar, *Austral. J. Agric. Res.*, 1956, **7**, 281; Gallagher, *Biochem. Pharmacol.*, 1960, **3**, 220.
[2] Crowley and Culvenor, *Austral. J. Chem.*, 1959, **12**, 694.
[3] Leonard, in Manske's "The Alkaloids," Academic Press, London, 1960, Vol. VI, p. 44.
[4] Munier, Machebouef, and Cherrier, *Bull. Soc. Chim. biol.*, 1952, **34**, 204.
[5] Waldi, *Arch. Pharm.*, 1959, **292**, 206.
[6] Curry and Powell, *Nature*, 1954, **173**, 1143.

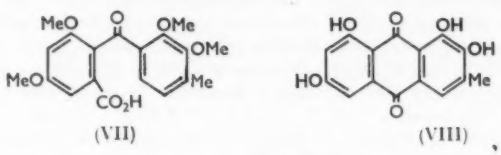
95. *Naturally Occurring Quinones. Part IV.*[1] *A Synthesis of Alaternin.*

By J. C. Lovie and R. H. Thomson.

The bark of *Rhamnus alaternus* L. contains an abundant mixture of hydroxyanthraquinone glycosides, of which emodin is the principal aglycone. A second pigment, alaternin, was isolated by Briggs and his co-workers [2] who deduced from chemical and spectroscopic evidence that it was a *C*-methyl derivative of 1,2,6,8-tetrahydroxyanthraquinone. On the assumption that the methyl group occupies the usual β-position, two structures are possible, the hydroxyemodin (VIII) being favoured on phytochemical grounds. This view is supported by the recent observation [3] that alaternin readily condenses with alkaline formaldehyde and we have now established structure (VIII) by synthesis.



An earlier attempt [1] to form 1,2,6,8-tetrahydroxy-3-methylanthraquinone by direct condensation of 3,5-dimethoxyphthalic anhydride with 3-methylcatechol was unsuccessful but our object has now been achieved by stepwise condensation of 3,5-dimethoxybenzoic ester with 2,3-dimethoxy-4-methylbenzoyl chloride. The latter was obtained *via* Fries rearrangement of 3-methylcatechol diacetate which gave a mixture of the two ketones (I) and (IV), containing 15—20% of the 1,2,3,4-isomer. Direct *C*-acetylation of 3-methylcatechol by boron trifluoride–acetic acid gave the ketone (I) with only a trace of the other isomer. The orientations are based on the infrared spectra of the isomers, the steam-volatility of the *o*-hydroxy-ketone, and the transformations shown in the formulæ. The anilide (III), obtained from the ketone (I) by Beckmann rearrangement of the oxime of its dimethyl ether (II), was identical with the product obtained by reductive acetylation of



3-methyl-5-nitroveratrole.[4] The *o*-hydroxy-ketone (IV) formed a dibenzoate (V) in pyridine solution which underwent a normal Baker–Venkataraman rearrangement to give the flavone (VI).

Methylation of the hydroxy-ketone (IV), followed by oxidation with hypobromite,

[1] Part III, *J.*, 1959, 4139.
[2] Briggs, Jacombs, and Nicholls, *J.*, 1953, 3069.
[3] Dave, Joshi, Patwardhan, and Venkataraman, *Tetrahedron Letters*, 1959, No. 6, 22.
[4] Majima and Okazaki, *Ber.*, 1916, **49**, 1482.

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yielded 2,3-dimethoxy-4-methylbenzoic acid which was used to acylate 3,5-dimethoxybenzoic ester. The resulting keto-acid (VII) was converted into 1,2,6,8-tetrahydroxy-3-methylanthraquinone (VIII) by brief treatment in molten aluminium chloride–sodium chloride. A sample of natural alaternin was not available to us but the infrared spectra of the natural and the synthetic material were kindly compared for us by Professor L. H. Briggs who reported that " there appears to be no significant difference between these two spectra and in our opinion the two compounds are identical."

Experimental.—*3-Methylcatechol diacetate* crystallised from light petroleum (b. p. 50—60°) in plates, m. p. 69° (Found: C, 63·4; H, 5·9. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%).

Fries rearrangement. 3-Methylcatechol diacetate (20 g.) was added to a molten mixture of anhydrous aluminium chloride (100 g.) and sodium chloride (20 g.) at 140°. The mixture was kept at 200° with continuous stirring for 30 min., cooled, and poured on ice and concentrated hydrochloric acid. Steam-distillation gave a yellow solid (3 g.) which after crystallisation from light petroleum (b. p. 50—60°) and sublimation at 60°/10 mm. afforded *2,3-dihydroxy-4-methylacetophenone* as pale yellow plates, m. p. 70° (Found: C, 64·9; H, 6·1. $C_9H_{10}O_3$ requires C, 65·0; H, 6·0%), $\nu_{max.}$ (in KBr) 1640 (chelated CO), 727 and 796 cm.$^{-1}$ (two adjacent ring C–H). The *dibenzoate* formed plates, m. p. 152—153° (from alcohol) (Found: C, 73·5; H, 4·8. $C_{23}H_{18}O_5$ requires C, 73·8; H, 4·8%). The *2,4-dinitrophenylhydrazone* crystallised from acetic acid in red needles, m. p. 288° (decomp.) (Found: C, 52·0; H, 4·2; N, 16·2. $C_{15}H_{14}N_4O_6$ requires C, 52·0; H, 4·0; N, 16·2%). *3,4-Dihydroxy-5-methylacetophenone* (8 g.) separated from the residual steam-distillation liquor on cooling. It crystallised from water (charcoal) in plates, m. p. 197—199° (Found: C, 64·9; H, 6·0%), $\nu_{max.}$ (in KBr) 1650 (CO), 862 and 882 cm.$^{-1}$ (isolated ring C–H). The *2,4-dinitrophenylhydrazone* formed red plates (from acetic acid), m. p. 268—270° (decomp.) (Found: C, 52·0; H, 4·0; N, 16·0%).

3,4-Dihydroxy-5-methylacetophenone was also obtained by warming 3-methylcatechol (3 g.) in boron trifluoride–acetic acid (15 ml.) at 60—70° for 3 hr. The mixture, after dilution with water (50 ml.) and addition of concentrated hydrochloric acid (5 ml.), was boiled for a few minutes and the resulting product (2·5 g.) collected. It crystallised from water (charcoal) in plates, m. p. and mixed m. p. 197—199°. Steam-distillation of the crude product yielded only a trace of the 1,2,3,4-isomer, m. p. and mixed m. p. 69—70°.

2,3-Dimethoxy-4-methylbenzoic acid. A solution of 2,3-dihydroxy-4-methylacetophenone (12 g.) in acetone (150 ml.) was refluxed for 9 hr. with dimethyl sulphate (25 ml.) and anhydrous potassium carbonate (80 g.). Working up gave the dimethoxy-ketone (11 g.), b. p. 138—140°/30 mm. This oil (1 g.) in dioxan (25 ml.) was treated with potassium hydroxide (3·5 g.) in water (13 ml.) containing bromine (1 ml.). After 1 hr., the solution was refluxed for 1 hr., and cooled. Sodium hydrogen sulphite (0·25 g.) and 8% aqueous potassium hydroxide solution (8 ml.) were then added, and the mixture was extracted thrice with ether. Acidification of the aqueous phase precipitated *2,3-dimethoxy-4-methylbenzoic acid* (1 g.) which crystallised from water (charcoal) in needles, m. p. 125° (Found: C, 61·4; H, 6·5. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·1%).

3,4-Dimethoxy-5-methylbenzoic acid. 3,4-Dihydroxy-5-methylacetophenone (4·5 g.) in acetone (100 ml.) was refluxed for 6 hr. with dimethyl sulphate (5 ml.) and potassium carbonate (20 g.). The *dimethoxy-ketone* crystallised from light petroleum (b. p. 50—60°) in needles, m. p. 47—48° (Found: C, 68·0; H, 7·4. $C_{11}H_{14}O_3$ requires C, 68·1; H, 7·2%). The *oxime* crystallised from light petroleum (b. p. 50—60°) (charcoal) in needles, m. p. 89—90° (Found: C, 63·0; H, 7·3; N, 6·6. $C_{11}H_{15}NO_3$ requires C, 63·2; H, 7·2; N, 6·7%). Hypobromite oxidation of the dimethoxy-ketone, as above, afforded *3,4-dimethoxy-5-methylbenzoic acid*, separating from water in needles, m. p. 151° (Found: C, 61·2; H, 6·2%).

3,4-Dimethoxy-5-methylacetanilide. (*a*) A mixture of 3,4-dimethoxy-5-methylacetophenone oxime (0·5 g.) and polyphosphoric acid (8 ml., 16·8 g.) was heated at 100° for 10 min., cooled, and poured into water (80 ml.). The *anilide* crystallised from light petroleum (b. p. 80—90°) in needles, m. p. 122° (Found: C, 63·0; H, 7·3; N, 6·5. $C_{11}H_{15}NO_3$ requires C, 63·2; H, 7·2; N, 6·7%).

(*b*) A solution of 3-methyl-5-nitroveratrole [4] (0·25 g.) in acetic anhydride (10 ml.) containing platinum oxide (0·05 g.) was shaken in hydrogen until absorption ceased. After filtration and removal of the solvent *in vacuo*, the residue crystallised from light petroleum (b. p. 80—

90°) (charcoal) in needles, m. p. 121° not depressed by admixture with the product obtained as in (*a*).

8-Hydroxy-7-methylflavone. Pulverised potassium hydroxide (0·7 g.) was added to a solution of 2,3-dibenzoyloxy-4-methylacetophenone (2 g.) in pyridine (7·5 ml.) at 50°. After being stirred at this temperature for 15 min. the mixture was cooled and acidified with 2N-acetic acid, to precipitate *2,3-dihydroxy-4-methyldibenzoylmethane* which separated from aqueous alcohol in yellow needles, m. p. 122—123° (Found: C, 70·8; H, 5·3. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%), $\nu_{max.}$ (in KBr) 1610 (CO of chelated β-diketone). This diketone (1 g.) in glacial acetic acid (30 ml.) was heated with concentrated sulphuric acid (1 ml.) on the steam-bath for 1½ hr., cooled, and poured on ice. The solid was collected and chromatographed in acetone on a magnesia column. The pale yellow *flavone* obtained on evaporation of the eluant crystallised from aqueous acetic acid in needles, m. p. 257—258° (Found: C, 75·7; H, 4·9. $C_{16}H_{12}O_3$ requires C, 76·2; H, 4·8%). The *methyl ether* crystallised from aqueous alcohol in pale yellow needles, m. p. 138—139° (Found: C, 76·5; H, 5·4; OMe, 10·8. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·3; OMe, 11·7%), $\lambda_{max.}$ (in EtOH) 260, 297, and 300 mμ (log ε 4·37, 4·29, 4·28 respectively); 8-methoxyflavone has $\lambda_{max.}$ 266, 299, and 301 mμ (log ε 4·33, 4·06, 4·05 respectively).

3,5-Dimethoxy-2-(2,3-dimethoxy-4-methylbenzoyl)benzoic acid. 2,3-Dimethoxy-4-methylbenzoic acid (3 g.) was refluxed for 30 min. with thionyl chloride (3 ml.). Excess of reagent was then removed under reduced pressure and the residual acid chloride was added in dry tetrachloroethane (20 ml.) to ethyl 3,5-dimethoxybenzoate (4 g.) in the same solvent (30 ml.). The mixture was stirred in an ice-bath while anhydrous aluminium chloride (2·7 g.) was added, in portions, during 30 min. After 2 hr. the ice-bath was removed and stirring was continued at room temperature overnight. The mixture was then poured on ice and concentrated hydrochloric acid. The aqueous phase was extracted with ether, and the organic phase steam-distilled to remove solvent, then extracted with ether. The combined ether solutions were evaporated, leaving a brown oil which gave a positive ferric reaction. Remethylation was effected by refluxing a solution of the oil in acetone with dimethyl sulphate (10 ml.) and anhydrous potassium carbonate (20 g.). The product, isolated in the usual way, was then hydrolysed by boiling with 2N-aqueous sodium hydroxide (150 ml.). The acid (4 g.) obtained on acidification crystallised from water in needles, m. p. 157° (Found: C, 63·1; H, 5·6. $C_{19}H_{20}O_7$ requires C, 63·3; H, 5·6%), $\nu_{max.}$ (in KBr) 1695 (carboxyl CO), 1660 cm.$^{-1}$ (diaryl CO).

1,2,6,8-Tetrahydroxy-3-methylanthraquinone. The above acid (1 g.) was added to a molten mixture of anhydrous aluminium chloride (10 g.) and sodium chloride (2 g.) at 120°. The temperature was rapidly raised to 180—190° and maintained for 3 min. with continuous stirring. After cooling, the mixture was poured on ice and concentrated hydrochloric acid, and after a few minutes' boiling the resulting precipitate was collected. Crystallisation from glacial acetic acid, followed by sublimation at 200—20°/2 × 10^{-5} mm., afforded red plates, m. p. 320—321° (Kofler) (lit.,[2] 310°) (0·4 g.) (Found: C, 61·6; H, 3·7. Calc. for $C_{15}H_{10}O_6$: C, 62·9; H, 3·5%). Despite repeated attempts, including purification through the tetra-acetate, a satisfactory carbon analysis could not be obtained. $\nu_{max.}$ (in Nujol) were at 758·5, 825·1, 863·5, 894·6w, 934·6, 1033, 1087, 1106, 1167, 1205, 1277, 1312, 1577, 1618, 3175, 3344. Natural alaternin has $\nu_{max.}$ 759·6, 826·4, 862·8, 886·1w, 905·3w, 934·6, 1033, 1087, 1107, 1206, 1277, 1319, 1572, 1613, 1686w, 3195, 3367. The tetra-acetate separated from alcohol in bright yellow needles, m. p. 222—223° (lit.,[2] 224°) (Found: C, 61·0; H, 4·2; Ac, 37·1. Calc. for $C_{23}H_{18}O_{10}$: C, 60·8; H, 4·0; Ac, 37·9%). The tetramethyl ether also crystallised from alcohol in yellow needles, m. p. 182° (lit.,[2] 181—182°) (Found: C, 66·8; H, 5·5; OMe, 37·2. Calc. for $C_{19}H_{18}O_6$: C, 66·7; H, 5·2; OMe, 36·3%), $\lambda_{max.}$ (in EtOH) 223, 277, and 365 mμ (log ε 4·30, 4·45, 3·81 respectively).

We thank Professor L. H. Briggs for the infrared data on alaternin, Dr. H. F. Bondy for supplies of 3-methylcatechol and Dr. T. H. Simpson for a sample of 8-methoxyflavone. One of us (J. C. L.) is grateful to the Department of Scientific and Industrial research for a Research Studentship.

THE UNIVERSITY, OLD ABERDEEN, SCOTLAND. [*Received, August 2nd,* 1960.]

XUM

96. *An Insect Repellant from Black Cocktail Ants.*

By C. W. L. Bevan, A. J. Birch, and H. Caswell.

Crematogaster (*Atopogyne*) *africana* Mayr. are a common West African species of black cocktail ant; they live on trees in roughly spherical carton nests made of chewed vegetable fibres mixed with a secretion of the maxillary glands of the workers.[1] When disturbed or crushed they give off a characteristic smell. This has been identified as due to hex-2-enal, which is an insect repellant also secreted by the cockroach *Eurycotis floridana*.[2]

Experimental.—Ants (100 g.) from a nest which was used as the source of specimens for identification were macerated under light petroleum (b. p. 60—80°; 100 ml.). This extract was then shaken with Brady's reagent, and the precipitated dinitrophenylhydrazone recrystallised from methanol; it had m. p. and mixed m. p. (with a synthetic specimen [3] of hex-2-enal dinitrophenylhydrazone) 142—143°. The infrared spectra of the dinitrophenylhydrazones taken in a Nujol film were identical; the ultraviolet absorption [$\lambda_{max.}$ 372 mμ (log ε 4·5) in chloroform] was consistent with that recorded [4] for hexenal dinitrophenylhydrazone.

We are indebted to Dr. Pearson of the Commonwealth Institute of Entomology for identification of the ants.

University College, Ibadan, Nigeria. [*Received, September 26th*, 1960.]

[1] Skaife, "African Insect Life," Longmans, Green and Co., London, 1953, p. 371.
[2] Roth, Niegisch, and Stahl, *Science*, 1956, **123**, 670.
[3] Ohoe and Hori, *J. Chem. Soc. Japan*, 1952, **73**, 275.
[4] Braude and Jones, *J.*, 1945, 498.

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